Staphylococcal Infections

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M D , CH B , F R F P S G

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PREFACE

IN THE HAPPY, carefree days of yesteryear when there was no specific treatment for infections many patients survived despite their treatment and the doctor usually got the credit In the past two decades many new effective drugs have been discovered to kill the bacteria which circulate in our communities With these powerful weapons comes added responsibility The infection must be correctly identified and the proper antibiotic must be given for an adequate time

Fortunately many infections such as streptococcal sore throat and pneumonococcal pneumonia are relatively easily recognized clinically and penicillin is a specific cure Recognition of staphylococcal infection is not usually difficult although many physicians do not always verify their clinical impression It is to be lamented that there is no single effective treatment which can be used in all cases but there are rules and clinical impressions to guide us

Originally the dramatic response of these infections to available antibiotics engendered a feeling of safety It is only in recent years that we have recognized both the renewed prevalence of staphylococcal infections and the increasing difficulty in curing them Some of these infections we cannot cure but the great majority can be treated with the agents now available provided a logical regimen is carried out This volume is an attempt to bring together the considerable knowledge available on the subject and in part to point out where further knowledge is re

quired It is for the physician in practice, and it will provide only essential references particularly to articles with useful bibliographies To those whose articles I have not mentioned, I offer my apologies but my aim has been to produce a clinical manual and not a reference text

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many times by Mrs Phyllis J Doane and Mrs Lucille Amish

In the preparation of the book the publishers have uncomplainingly made repeated changes, but nonetheless they have gone from the typewritten manuscript to the published book in a very short time I wish to thank them for their unfailing help

I M S

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IN JUST one year staphylococcal infections were responsible directly or indirectly for 129 of approximately 750 deaths in our hospital Staphylococci that previously were thought to be ubiquitous and not too harmful parasites now demand our attention. Cross-infections have visited us in the past, and the belief grew that antibiotics were the answer to this problem Increased morbidity and mortality from staphylococcal sepsis show this idea to be false

Staphylococcal infections differ from other infections in several ways. They form localized abscesses in which rapid necrosis occurs and additional destruction of tissue follows the thrombosis of neighboring capillaries The organisms are versatile chemical factories If it were not so they would not have defied our many new antibiotics In the nooks and crannies of the body staphylococci persist, to multiply when conditions become more favorable Immunity if it does occur is transient and poor in quality

We are seeing more staphylococcal disease Post antibiotic staphylococcal enteritis is a new entity Epidemics have occurred in hospitals usually with a hardy strain resistant to many antibiotics The way has been prepared for these outbreaks by an indiscriminate use of antibiotics which has removed all susceptible (possibly protective?) staphylococci from the anterior nares where they are carried

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For these several reasons the time has come to collect evaluate the knowledge concerning staphylococci which is s tered throughout many books and journals

THE GIST OF THE BACTERIOLOGY

Ogston a Scottish surgeon who first described the staphyl cocci in 1881 noted that they grow in pus in grapelike cluster They divide in two planes in contradistinction to streptococ which divide in a single plane and grow in chains.

The staphylococci* are spherical bacteria which occur in pair tetrads and clusters, are nonmotile and are Gram positive Ar amino acid source of nitrogen is required for their growth Ir broth a uniform turbidity and a slight ring pellicle around the top develop Although staphylococci grow well without oxygen they grow better in its presence They like best a temperature of 37 C but will grow between 10–45°C A special characteristic of staphylococci is their property of growing in media containing 10% sodium chloride

Staphylococci grow readily on the usual laboratory media Sheep or horse blood agar is probably the medium most fre quently used Smooth round opaque moist shiny domed, oil paintlike colonies 2–3 mm in diameter grow within 18–24 hours after inoculation The colonies are often surrounded by a clear zone of hemolysis They develop a characteristic golden (*aureus* strain) a porcelain white (*albus* strain) or rarely a lemon yellow color (*citreus* strain) The aureus variety cause

*The time honored names staphylococci has with official sanction returned to the bacteriological literature in place of the confusing micrococcus Recently however it has been suggested that, because chromogenesis may be difficult to identify and is not always a stable characteristic, all varieties should be called *Staphylococcus pyogenes* As clinical medicine deals in probabilities rather than in certainties I find chromogenesis enough of a help in dealing with disease in the individual patient to wish to retain it. Throughout the book I have referred therefore to *Staphylococcus aureus* and *Staphylococcus albus* believing that the benefit of this method outweighs its limitations

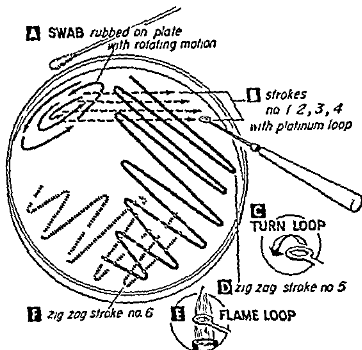


FIG 1 —The correct method of plating a nose swab The numbers indicate the successive strokes of a platinum loop

most infections It is important to remember however that pigment formation may be delayed Spreading a colony on white filter paper and allowing it to dry is the most satisfactory method for detecting the pigment If there is any doubt further incubation at room temperature will help in this assessment.

To obtain discrete colonies plates should be properly streaked as shown in Figure 1

A *Gram stained preparation* shows cocci of uniform size in clusters Typically these cocci are Gram positive Some strains

under certain conditions stain poorly, and many of the bacteria will be Gram negative Strains stored in the laboratory tend to become Gram negative

ARE ALL THE STAPHYLOCOCCI THE SAME?

A strain of staphylococcus may be of the aureus type, hemolytic, coagulase, positive, and it may ferment mannitol (*vide infra*), yet it still may differ from another strain with the same biochemical characteristics The most satisfactory method of identifying staphylococci is the bacteriophage typing method This is laborious but rewarding

The bacteriophage a living viral parasite is found in nature associated with staphylococci The several varieties of phage can be kept alive in the laboratory by growth on carrier staphylo cocci To type an unknown staphylococcus an agar plate is flooded with a young culture of the unknown strain and the excess is removed After drying the surface of the plate 1 drop of each of the 24 commonly used phages (Table 1 and Fig 2) is

TABLE 1

Group I	Phages 29 29A 52 52A 79 80
Group II	Phages 3A 3B 3C 51 55 71
Group III	Phages 6 7 42B 42E 47 47B 47C 53 54 70 73 75 76 77
Group IV	Phage 42D
Miscellaneous	Phages 31 42C 44 44A, 47A 57 81 VA4

placed on the plate in a predetermined order and this is allowed to incubate Upon examination it will be found that one or several of the areas treated with phage the surface growth of the staphylococcus has been completely or partly cleared (Fig 2) This is

NOTE Staphylococcal strains n group I 70-30% e istant t penicill nly occasional strains are resista t to tr ptomyci Less tha 10% of gro p II strai are resista t to penicilli t ptomyci the t tracycl or hl ramph nicol Gro p IV t ains are rare in man and a e t resista t to ant b t cs Strains respo s bl f h p tal acquired infections are pred min tely of phag group III a d m t of th m are resi ta t to peni cillin treptomycin d the tetracyclin s.

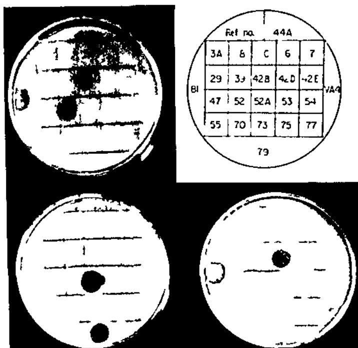


Fig. 2.—*Above right*, key to the placement of the numbered phages. *Above left*, phage type 42B/52/81 staphylococcus obtained from a breast abscess in a nurse. *Below left*, phage type 52A/79 staphylococcus obtained from a wound infection in a patient cared for by this nurse. *Below right*, phage type 42B/52/81 staphylococcus obtained from the nose of the nurse's husband, a physician. Note that the 52 reaction is weak but definite. It is reasonable to assume that the patient did not acquire his wound infection from the nurse and that the nurse's frequent bouts of sepsis despite adequate chemotherapy are due to reinfection from the reservoir of organisms in her husband's nose.

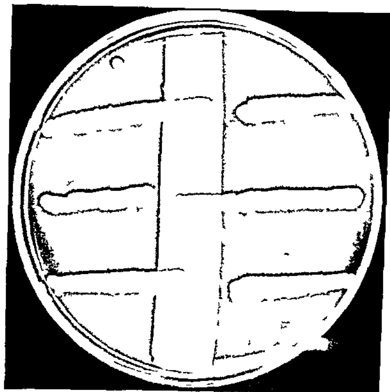


FIG 3—Duplicate tests on three staphylococcal strains showing antigen antibody flocculation lines

caused by the rupture of the growing cells from the multiplication of the viral parasite Staphylococci are seldom lysed by a single phage and are therefore referred to by their phage pattern for example 6/47 or 42B/81 Strains that differ by more than 2 phage reactions are considered to be distinct from one another These patterns are stable and by this method it has been possible to show that there are many strains within the staphylococcal family group

WHAT IS STRAIN 80 OR 81?

Since 1953 a strain of phage type 80 or 81 with or without additional phage reactions (e.g 42B/55/81), has been isolated with increasing frequency in outbreaks in hospitals in Australia, Europe Britain and the Americas. This strain is resistant to the commonly used antibiotics Recently it has even caused a few infections in general practice, particularly in the families of physicians. Follow up studies on outbreaks of staphylococcal sepsis in newborn nurseries have also shown the spread of this strain and other hospital acquired strains in homes in the United States Although strain 80 and strain 81 are not identical, they are nearly so, and they are vastly in the majority among hospital strains.

Is This Strain Dangerous?

Two types of tests are used to determine the disease producing potentialities of a strain In the first test, one particular chemical reaction produced by the staphylococcus is studied, and its presence is related to the ability of the strains to cause severe disease In the second reliance is put on the combined action of a group of chemicals or toxins

TESTS FOR SINGLE TOXINS

Production of coagulase —This is a valuable test to identify possibly dangerous strains Most staphylococci which produce virulent disease in humans produce an enzyme which will coagulate plasma In the standard test plasma is obtained from the rabbit To ½ cc of this plasma diluted 1 in 10 is added 1 drop of overnight culture of the staphylococcus to be tested This mixture is incubated for 3–4 hours and then examined A clot indicates the production of coagulase any degree of clotting is a positive result Since a few strains do not clot within this period the reading should be checked 24 hours later It has been found

that 96% of strains causing virulent disease in humans can be counted on to produce coagulase if oxalated plasma is used False positive results are not obtained with other gram positive cocci An occasional coagulase producing strain of pseudomonas or *E coli* is found Very rarely false negative results might occur due to contamination with a fibrinolytic organism

A presumptive test for coagulase called the slide test has been devised In this test a small portion of a colony is emulsified in rabbit plasma and if clumping occurs within 30 seconds or less coagulase is presumed to be present It has been shown that the clumping factor is distinct from the coagulase factor but that they parallel each other very closely

A useful method in the routine laboratory is to streak staphylo cocci on infusion agar plates which contain 16% V/V of human plasma After 24–hours incubation, coagulase positive strains show a cloudy zone around the colonies Another screening test is to grow the colonies on agar containing phenolphthalein di phosphate Phosphatase which is constantly found in coagulase positive organisms splits off the phenolphthalein When exposed to strong ammonia coagulase positive strains become red in color

Production of hemolysin —Five different types of hemoly sin are produced by the staphylococcus alpha beta gamma delta and epsilon hemolysins In man the important one is the α hemolysin this lyses rabbit and sheep red blood cells under aerobic but not anaerobic conditions Ninety four per cent of the strains virulent in humans produce this α hemolysin Staphylo cocci from infected animals produce more β hemolysin than those from human sources (see Chapter 8) Production of hemolysis in blood agar plates is only suggestive of production of α hemolysin and is only roughly correlated with virulence in humans

Fermentation of mannitol —Mannitol is a sweet tasting carbohydrate obtained from many fungi or from the dried exu date of manna Most virulent staphylococci ferment mannitol with the production of acid but not of gas A correlation between mannitol production and virulence of the strain in man gives less

satisfactory results than either the production of coagulase or of α hemolysin The other fermentative reactions of staphylococci are of no practical importance

TESTS FOR MULTIPLE TOXINS

VIRULENCE IN ANIMALS —Intravenous inoculation in rabbits has been used in the past for the assessment of virulence When death occurs in animals it is usually due to the strain being aureus in type The length of time between inoculation and death will indicate virulence A strain which in a small standardized dose kills rabbits within 2 days belongs to a virulent group

Mice are easier and cheaper to keep than rabbits and have been used recently in my laboratory for testing strains of staphylococci Mice are killed by aureus but not by albus strains A strain which given by the intravenous route will kill more than 50% of a group of 10 mice within 2 days is likely to cause severe disease in the person from whom it was obtained The intraperito neal route which is simpler to do may also be a method for test ing the virulence of staphylococci in mice It requires more study

ANTIGEN ANTIBODY FLOCCULATION TEST —Figure 3 illustrates this test clearly The strains of staphylococci to be tested are streaked across the agar at right angles to a strip of filter paper soaked in antitoxin which lies embedded in an agar plate Anti toxin diffuses up through the agar and meets toxin which diffuses down from the organisms being tested When a suitable concen tration of each is reached a linear precipitate forms The number of lines indicates the number of toxins produced provided that these toxins form precipitating antibody and that they are present in the antitoxin used This test has been found to show a clear relationship to the virulence of the strain in animals or in man It has recently been suggested that degradation of a carrier strain increases according to the length of time it is carried in the nose This results in a decrease in virulence and in a corresponding de crease in antigen antibody flocculation lines

SENSITIVITY AND RESISTANCE TO ANTIBIOTICS

Tests for antibiotic sensitivity are best carried out as tube dilutions tests. Due to the pressure of work, however, many laboratories use the less accurate but still useful method of disk sensitivity testing.

In hospitals many strains are resistant to the commonly used antibiotics. In the general population outside hospitals, however, many penicillin-sensitive strains remain. It is unusual for a staphylococcus to change its antibiotic sensitivities during treatment. When this appears to happen, phage typing usually shows that the original strain has been replaced by another strain of different phage pattern and of different antibiotic sensitivities.

WHAT DOES RESISTANCE TO EVERYTHING MEAN?

Strains of staphylococci which are concurrently resistant to penicillin, streptomycin, tetracycline and perhaps erythromycin have frequently been acquired in hospital. A limited number of strains thus developed are transferred by cross infection. This resistance does not reflect virulence, but these organisms may multiply because of mistakes in chemotherapy.

SEROLOGICAL TESTS

Various serological tests have been tried and are being tried today. So far, no clinically useful test has been developed.

ESSENTIALS OF THE EPIDEMIOLOGY OF STAPHYLOCOCCI

Staphylococci are not present in the nose, throat or on the skin at birth: they appear in the nasopharynx in the early weeks of life. Within 2 weeks of birth almost every child acquires staphylococci in the anterior nares. (Incidentally, these staphylococci are not *all* coagulase positive.) More coagulase positive staphylo-

cocci are found in children born in hospitals than in those born at home and careful studies of the antibiotic resistance and the phage type of these organisms indicate that they are more often obtained from the nose of an attending nurse or physician than from members of the children s own families If infection occurs at all the usual sequence is that the infant develops a purulent eye in the second or third week following delivery Later the mother may develop a breast abscess

After the first month of life the carrier rate falls until at the age of 6 months only 23% of children have staphylococci in their noses. From this age the incidence increases until among adults it is approximately 70% Not all of these staphylococci found in the noses of the adult population are coagulase positive and potential disease producers, but this type of potentially virulent organism is carried by approximately 30% of the population The per cent incidence of carriers is greater in hospital environ ments than among the general public Some people who are nasal carriers also have staphylococci in their feces or on their skin or both A few people carry the organisms on the skin without being nasal carriers but this is rare

Patients entering a hospital only occasionally bear coagulase positive staphylococci The per cent occurrence of these carriers rises with the number of weeks spent in the hospital

Staphylococci do not cause many diseases in domestic animals There is no great focus except in man *The main area for growth in man is the human nose* It is obvious from watching any group of people that many people frequently pick or otherwise handle their noses and in this way spread staphylococci to handkerchiefs clothing bed clothes and other objects

ARE STAPHYLOCOCCI PART OF THE NORMAL FLORA OF THE BODY?

In the years between 1890 and 1900 when the tuberculin test was first used most people had skin reactions to it If a positive

tuberculin test means live tubercle bacilli in the body, then tu bercle bacilli at that time were part of the normal flora of the body Now it is considered that a positive tuberculin test is an abnormal undesirable development

We cannot yet say whether *Staphylococcus aureus* is part of the normal flora of the body When we have a constantly effective bactericidal drug, a re assessment of this problem can be made At the present time a culture of *Staphylococcus aureus* from any area other than the intact skin or the anterior nares or pharynx must be considered abnormal It should be correlated with other evidence of disease

STAPHYLOCOCCAL INFECTION IN THE GENERAL POPULATION

Eighty per cent of people suffer from staphylococcal sepsis sometime during their life and in any one year 5% have a staphy lococcal lesion The strains found are predominantly sensitive to penicillin and rarely resistant to other antibiotics *unless* the in dividual was recently discharged from hospital

In some an entrenched family infection occurs A history of styes, boils carbuncles or other septic lesions in relatives before and after infection in a patient may explain recurrent relapses

THE CONTROL OF STAPHYLOCOCCAL INFECTIONS IN HOSPITALS

SURVEYS —The first step in control must be a careful assess ment of the extent of the problem in any hospital It has been shown that a *ward round type of survey* checking for known staphylococcal disease and checking the bacteriological records on the patients will give a good indication of the amount of staphylococcal disease prevalent in any hospital More detailed surveys, involving the culturing of noses of patients and attend ants, are expensive and very time consuming A very useful check is to examine all autopsy records for a particular year provided

that cultures for staphylococci have been taken routinely from heart blood and from obvious pus-forming lesions. Such surveys done in our hospital showed that an average of about 15% of the patients on all services had pus-producing staphylococcal lesions and that 4% of patients in one year died directly from staphylococcal infections Another 14% of patients deaths was contributed to by a staphylococcal infection

Serious outbreaks such as those occurring in a newborn nursery or postoperative ward require more detailed investigation. All personnel and patients should be examined ideally with nose anal and skin swabs However for practical purposes nose swabs are the most important. Phage typing of the strains obtained may indicate the source of an outbreak. With serious outbreaks an additional method of survey is to use an air sampler whereby air at a definite rate is impinged on a plate and the coagulase positive staphylococci are counted. It has been found that in clean wards there is an average of 1 colony per 100 cu ft. and in dirty wards there is somewhere in the neighborhood of 35 colonies per 100 cu ft. Similar figures have been obtained for contaminated and clean operating rooms

The above mentioned methods of appraisal are suitable for *production control* a system of checks such as are used in industry to control the manufacture of a product. A checking routine of this nature is needed in most hospitals to make sure that the recommended procedures for the avoidance of cross-infection are being used Such surveys and the recommendations for dealing with an outbreak are best made by a particular individual who is interested in infectious disease or alternatively by a committee formed of people from different services in the hospital

Another method is *notification control* This means notifying all personnel of all staphylococcal diseases occurring in the hospital. This will remind all the personnel involved of the magnitude of the problem.

A patient may develop a staphylococcal infection after discharge from the hospital since the peak time for acquisition of

endemic hospital strains is 10 days after admission, and many patients are discharged before this This part of an outbreak can be discovered by *telephone surveys* Trained workers call patients who have been recently discharged from the hospital and inquire regarding pus producing lesions

ISOLATION OF INCOMING SEPTIC PATIENTS —Some form of isolation should be devised for incoming patients with wounds that are contaminated with staphylococci Patients who are coughing up copious quantities of purulent sputum containing staphylococci should receive complete respiratory isolation A patient with an open lesion containing pus with staphylococci can be isolated by the application of an occlusive dressing All concerned with patient care should take extra precautions if charts and treatment cards are stamped staphylococcal infection Although carriers are an ever present threat in a hospital, an open case of staphylococcal infection is a more potent source of a ward outbreak

HANDWASHING —Probably the most important single factor *in controlling staphylococcal infections in hospitals is hand* washing In many cases our hospital plumbing is inadequate Many people do not realize the importance of washing their hands between the treatment of infected patients This does not mean a surgical scrub but a careful washing with a suitable agent Hexachlorophene soap is easily dispensed in liquid form from a foot controlled container Hand basins should have foot controls for the water

Antiseptic hand cream has been used in the control of some outbreaks One compound used 1 6 di 4′ chlorophenyldiguanido hexane 10,040 is marketed in Britain by Imperial Chemical (Pharmaceuticals) Limited as Hibitane This material caused a great decrease in resident bacteria or contaminating bacteria on the hands with a *decrease in staphylococcal cross-infection* in a maternity unit

CARRIERS —The carriers of coagulase positive staphylococci are a very important danger in the spread of hospital infections

In nine cases out of ten carriers can be identified by a single nose swab During an outbreak carriers should be located All carriers cannot be treated for they may make up almost one half of the personnel in any hospital Furthermore antibiotic treatment will cause the staphylococci remaining in the hospital to become resistant to this agent Persistent carriers can be treated but this involves a great deal of work and additional personnel for this investigation are not usually available A quicker and easier method for identifying carriers of coagulase positive staphylococci is needed before better control can be carried out It has been shown that a certain per cent of hospital personnel persistently carry coagulase positive staphylococci and that a certain per cent consistently do *not* carry coagulase positive staphylococci If people in hospitals are followed for a long period it can be shown that all of them at some time carry a staphylococcus but that it is not necessarily coagulase positive The best way to deal with carriers is to educate all hospital personnel Everyone should be instructed to act as if he was a carrier which means using no touch techniques masks and gloves An exception to the nontreatment of staphylococcal carriers is made in the case of a dangerous carrier This is a person known by phage typing to be the source of an outbreak of staphylococcal infection In this case antibiotic treatment locally systemically or both is justified

Wound dressing —Contaminated wounds should be dressed in one room and clean wounds in another Both rooms should be air conditioned and have electrostatic precipitors Gloves and masks which have an impervious layer between the gauze should be worn A no touch technique using forceps is advisable The control of wound dressing should include the keeping of a wound book in which the state of all wounds is recorded In the past good results have been obtained by leaving clean wounds uncovered after operation as organisms grow easily in the sweat and serum retained by dressings

Operating room technique —A mild positive pressure

should be maintained inside the theater so that all air leaks outward It helps to have operations carried out as soon as practicable after admission since a large number of patients acquire the hospital staphylococcus about 10 days after admission Operating room personnel should have their skin inspected for septic lesions at regular intervals and personnel with infections should be excluded Special operating room clothes should be worn within the operating room area but *not* outside of it Shoes should be changed because they may transfer infected dust from the wards *The mask and the cap of each operator should be changed* between operations No blankets from the ward should be brought into the operating room Traffic in and out the operating room stirs up dust containing organisms and should be reduced to a minimum To decrease movement within the theater seats should be provided for those working therein At the time of operation, organisms can be introduced by glove puncture or by transmission from the skin through wet sleeves of operators Improperly worn masks also contribute to wound contamination Ideally septic cases should be treated in a separate operating room Alternatively, all the operations on septic cases should be at the end of the day s schedule

CHILDREN S WARDS —Children should not be admitted to the hospital for trivial illnesses Children are particularly susceptible to staphylococcal disease and disseminated staphylococcal disease has a moderately high mortality in childhood To avoid hospital contamination of the newborn the best method is to consider the mother and the baby as one unit and to have as much as possible done by the mother rather than by a nurse Others handling a child must consider themselves as carriers and behave accordingly

THE DIAGNOSIS AND TREATMENT OF STAPHYLOCOCCAL INFECTIONS —All sepsis occurring in the ward should be suspected of being staphylococcal Physicians working in a hospital would do well to know the current sensitivities of the strains prevalent in their own hospital It is important however to take cultures so

that this impression can be confirmed or corrected by in vitro sensitivities Appropriate treatment should be started promptly in serious cases

ADMINISTRATION AND HOUSEKEEPING IN REGARD TO STAPHYLOCOCCAL INFECTIONS —The large open undivided ward has become obsolete Adequate plumbing and numerous sinks to help in the washing of hands are mandatory for the control of staphylococcal infections Dry mopping and sweeping should be avoided as these activities mobilize a large number of dust particles carrying infectious material Overcrowding should be avoided beds should have 80 square feet of floor space as recommended by the American Hospital Association or else there should be 8–12 feet between bed centers as recommended by the British Medical Research Council

Blankets are a particularly common source of organisms Blankets may be treated by light oiling so that bacteria will stick to the fibers during bed making instead of being scattered It is possible to do this oiling at the time of laundering but this process is expensive and has not gained general acceptance Alternatively blankets may be treated with a quaternary ammonium compound in the rinsing water Boiling blankets is preferable to either of these treatments as it kills tubercle bacilli and pseudomonas as well as staphylococci (Both the towelling type of blanket and the cotton weave blanket may be boiled Woolen blankets shrink over 30% and become felted and hard with this treatment) Mattresses and pillows should be covered with impermeable rubber or plastic and the covers should be treated by autoclaving boiling or some form of cold sterilization Since infection spreads in dust particular care should be taken to avoid contaminating walls and other areas After discharge of an infected patient decontamination of these areas by the standard methods is recommended All contaminated linen should be autoclaved before sorting and counting after this it may be laundered in the usual fashion

THE COST OF INFECTION AND THE PRICE OF CONTROL —A study of the additional expense both to the patient and to the hospital

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for staphylococcal infection should rarely be necessary if rules are obeyed

WITHDRAWAL OF A DRUG FROM USE —In New Zealand erythromycin has been withdrawn from general use and is reserved for hospital use for cases of serious staphylococcal disease only The results of this large scale experiment will be of great interest. On a *smaller scale it has been shown that the widespread use of a new* antibiotic (erythromycin) can lead to the rapid production of resistance to this agent When such a drug is withdrawn the high level of resistance declines very slowly and even more than a year later it has not returned to its earlier level The education of the staff in the use of antibiotics is therefore much preferred to the banning of the use of one drug The newly introduced antibiotics which can only be used intravenously will rarely be used and therefore they will probably maintain their efficacy

THE ABUSE OF ANTIBIOTICS —The indiscriminate use of antibiotics leads to the more frequent production of carriers of antibiotic resistant staphylococci than does the carefully planned use of these agents Usually only one phage type of staphylococci is isolated from a carrier Many people carry nonpathogenic coagulase negative or coagulase positive staphylococci of relatively low virulence which are sensitive to the common antibiotics It is better to keep the staphylococcus one has than to sterilize the nasal mucosa and then be in a condition to receive the current epidemic strain in the hospital

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(Table 2) indicates that if staphylococcal infections could be prevented there would be a considerable financial as well as medical gain Money spent in hospital alterations and the chang ing of equipment is therefore well invested

TABLE 2 —THE COST OF INFECTION WITH STAPHYLOCOCCI

Diagnosis	Uncomplicated		With Staphylococcal Infection	
	Length of Stay in Days	Cost† in Dollars	Length of Stay in Days	Cost† Dollars
Adenocarcinoma of breast	13	256	40	809
Adenocarcinoma of breast	14	294	38	954
Adenocarcinoma of breast	23	444		
Fracture of hip	10	274	57	1 347
Fracture of hip	12	416		
Benign prostatic hypertrophy	12	353	37	672
Benign prostatic hypertrophy	21	498		

P ti nts were match d fo g sex and type of lesion.
†Includes room and board, operati g room anesthesia, x ray laboratory drugs, and oxyge charges but not any physicians f es.
I am indebted to Mr William W dell for these figures.

EDUCATION —Education begins first with the physician and he must see that it permeates the whole staff Staff physicians first of all should protect themselves against contamination and in fection. Physicians and house staff should be required to observe isolation rules Many auxiliary personnel have no training in hygiene and so they must receive specific instruction. The first rule is asepsis for all procedures of a surgical nature whether major or minor The next rule to emphasize is washing the hands. Any staff members who have furuncles or other septic infections should be kept off duty A previous practice of transferring per sonnel so infected to a medical service can no longer be consid ered correct. Special care must be given to those who are suscep tible to staphylococcal infections namely the debilitated and infants. When all concerned behave as if they are carriers hospi tal acquired infections will be greatly reduced. Closure of a ward

for staphylococcal infection should rarely be necessary if rules are obeyed

WITHDRAWAL OF A DRUG FROM USE —In New Zealand erythromycin has been withdrawn from general use and is reserved for hospital use for cases of serious staphylococcal disease only The results of this large scale experiment will be of great interest On a smaller scale it has been shown that the widespread use of a new antibiotic (erythromycin) can lead to the rapid production of resistance to this agent When such a drug is withdrawn the high level of resistance declines very slowly and even more than a year later it has not returned to its earlier level The education of the staff in the use of antibiotics is therefore much preferred to the banning of the use of one drug The newly introduced antibiotics which can only be used intravenously will rarely be used and therefore they will probably maintain their efficacy

THE ABUSE OF ANTIBIOTICS —The indiscriminate use of antibiotics leads to the more frequent production of carriers of antibiotic resistant staphylococci than does the carefully planned use of these agents Usually only one phage type of staphylococci is isolated from a carrier Many people carry nonpathogenic coagulase negative or coagulase positive staphylococci of relatively low virulence which are sensitive to the common antibiotics It is better to keep the staphylococcus one has than to sterilize the nasal mucosa and then be in a condition to receive the current epidemic strain in the hospital

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2 / DISEASES OF THE SKIN

STAPHYLOCOCCAL infection of the skin affects all age groups Some lesions heal if the skin is kept dry and if early lesions are covered with an occlusive dressing other lesions demand the utmost clinical skill and antibiotic therapy for their cure

PUSTULES IN INFANTS

In recent years an increase in the number of cases of minor kin infections of newborn infants has been noted About 5% of the children born at home and 10% of those born in the hospital will develop staphylococcal pustules We find that these pustules are four times as frequent in premature infants as in full term ones After the first month of life the incidence of skin sepsis falls sharply

The infection varies in type from small pustules to extensive bullous impetigo (pemphigus neonatorum) The lesions usually consist of superficial easily broken vesicles on a reddened base occurring singly or in groups Outbreaks of this disease are a real danger sign for they indicate lax standards of infant care however they are *not* an indication for the automatic use of antibiotics since 80–90% of the cases can be controlled without drugs

TREATMENT *—The best way to treat these pustules is to cover each lesion The covering will prevent their spreading and pro

*A detailed description of the treatment of all types of staphylococcal disease is found in Chapter 9

mote healing Systemic antibiotic treatment needs to be considered only when a constitutional reaction occurs. Topical antibiotic creams may be beneficial though not usually required an ointment of ammoniated mercury is a useful nonantibiotic agent to use

MULTIPLE SWEAT GLAND ABSCESSES OF INFANTS

SYNONYMS —Multiple subcutaneous abscesses in infants folliculitis abscedens infantum periporitis staphylogenes

PATHOLOGY —In babies the sweat glands have wide openings which are easily infected although the follicles seem to be immune to infection Abscesses in sweat glands thus correspond to furuncles in adults On section one sees a subacute almost granulomatous inflammation centering around the sweat coils Leukocytes histiocytes in large numbers and cocci can be demonstrated in the purulent exudate around the sweat coils

BACTERIOLOGY —*Staphylococcus aureus* or *Staphylococcus albus* can be obtained from pus from these lesions In a few infants there is a bacteremia

PREDISPOSING FACTORS —Undernourishment is characteristic of many children with this infection The infection occurs mainly in hospital born children The disease is rare

CLINICAL FEATURES —The affected child is usually under 18 months of age Small lumps appear in the occipital region, on the back or on the buttocks The lumps are deep seated and have normal overlying skin There may be 20–30 lesions varying in diameter from 1–5 cm They become dusky red, fluctuant dome shaped superficial abscesses without the central plug of a furuncle

TREATMENT —Long term (up to 6 weeks) antibiotic treatment is recommended with an agent shown to be effective against the staphylococci isolated Incision and drainage is not usually necessary

INFECTED ACNE

PATHOLOGY BACTERIOLOGY AND CLINICAL FEATURES —This is a disease of young adults from puberty to ages 25–30 Cells and sebum accumulate at the mouths of sebaceous glands turn black and form the basic lesion of acne the comedo The latter may be infected with coagulase positive staphylococci causing first a red inflammatory halo and then a pustule In other patients the acne is infected with *Staphylococcus albus* A majority of teen age chil dren have some acne The hormonal changes of puberty are prob ably connected with this as both ACTH and testosterone can produce acneform lesions (mostly keratinization) in predisposed persons

ACNE CONGLOBATA.—(*Conglobata* means massed or clumped) Deep abscesses with interconnecting and draining sinuses may develop as complications of acne if the mouths of the follicles are blocked Double and triple comedones are common

TREATMENT —Exfoliation produced by sulfur (2–15%) or resorcinol (1–4%) compounds in liquid vehicles is beneficial The use of hexachlorophene soap or 70% alcohol rubbings also helps Steaming of the face followed by gentle comedo expression is a basic part of treatment and it also improves the cosmetic result

Chocolate and other dietary elements may be harmful to some patients with acne this is substantiated by our recent dietary ex periments in mice infected with staphylococci. Rigorous elimina tion dietary treatment is not indicated but the elimination of dietary agents known by the patient to cause an exacerbation is helpful Adequate amounts of exercise and sunlight are beneficial

Pustular lesions require drainage with carefully planned stab-type incisions In acne conglobata the tunneled lesions require unroofing in their entire course

Antibacterial treatment is not needed in the majority of cases but in certain deep pustular types it should be prolonged Re

tained secretions containing staphylococci permit recurrence following short term therapy If the strain is sensitive tetracycline is a good agent for this purpose Erythromycin is another That the nose is a focus for staphylococci should be explained to the patient Staphylococci obtained from the nose should also be examined for antibiotic sensitivities and local treatment given

Toxoid has been used with benefit in the treatment of pustular acne After skin testing with 0 5 ml of a 1 10 dilution, 0 1, 0 2 0 4 0 8 and 1 0 ml of the toxoid are given at intervals over a 3 week period Injection of this material causes an ache at the site of injection and in neighboring areas for 12–72 hours, increasing in severity with the dosage Headache is also frequent. Benefit is not usually noted until more than 3 months later It is probably best reserved for intractable cases

IMPETIGO

BACTERIOLOGY —*Staphylococcus aureus* has been grown in 81% of lesions *Streptococcus pyogenes* alone in 6%, and a mixed growth of both in 13% Impetigo is a specific infection which breeds true It is not contracted from patients with boils nor does it usually give rise to pyogenic lesions of other kinds Among the staphylococcal group of impetigo cases it is now known that over 80% are caused by phage type 71

CLINICAL FEATURES —Impetigo is usually a disease of school children although young adults particularly males are also affected It is a pustular disease of the skin of the face usually originating near the anterior nares and spreading across the face to form honey yellow crusts which appear to be stuck on When these crusts are removed a reddened weeping surface is present underneath Spread of the disease occurs quite frequently into the anterior nares Children may have pustular lesions of the finger similar in type to those on the face Also in children this disease quite frequently follows measles chickenpox or herpes simplex. In newborn children impetigo which is usually acquired

from a carrier may occur around the area of the umbilicus

Impetigo is contagious in the newborn and young adults only. It shows very little tendency to spread in older people.

In the few cases due to streptococci the lesions are different. There is an erythematous zone around the crusts which are very large and yellow, and the base has a white sodden appearance.

Pemphigus neonatorum is a spreading bullous type of impetigo.

TREATMENT.—Before effective remedies can reach the infected lesions the crusts must be removed. They can be softened with warm saline solution and then gently removed with forceps. Soaks of ¼% acetic acid (3 tablespoonfuls of vinegar to 1 quart of water) or half saturated boric acid are also effective and moderately bactericidal. Salicylic acid or menthol in local applications or aspirin systemically helps to allay itching. The base of the ulcer can be treated with ammoniated mercury ointment, bacitracin, neomycin or polysporin ointment.

SCARLET FEVER FOLLOWING ANTIBIOTIC TREATMENT

Children in the 1–10 age group may develop a disease indistinguishable from scarlet fever about 5 days after receiving tetracycline or one of its derivatives.

INCIDENCE.—About 3% of children in one series treated with the tetracyclines developed scarlet fever. A further 7% developed sore throat without rash.

BACTERIOLOGY.—Coagulase positive staphylococci are found in the throat in the absence of β hemolytic streptococci.

CLINICAL FEATURES.—The child has a sore throat and a temperature of 102–103° F. The rash is a punctate erythema of the trunk and the face is flushed except for an area of pallor around the mouth. The throat and palate are edematous and show patchy white exudate which may become confluent. Other children treated with tetracycline develop only the sore throat.

TREATMENT.—Full dosage systemic antibiotic treatment for

2 weeks is recommended with an agent shown to be effective by in vitro tests Isolation is necessary

PROGNOSIS —The disease is not fatal and usually responds within a week to the above treatment

FURUNCLES

Boils occur equally in both sexes except that men have boils on the back of the neck more often than women do There is a peak of incidence in the months of October and November al though boils may occur at any time of the year These patients have a staphylococcus in their noses of the same phage type as that causing the boils The hands remove the staphylococci from the nose and deposit them at areas of irritation by scratching Itching of the site of the boils may occur at the same time as the onset of the boils or sometimes it is stated by the patient that itching preceded the boils

As a boil is an infection of the hair follicle, it can only occur on hairy surfaces Friction and maceration predispose The boils occur most often on the face, head neck forearms and wrists in that order although any area except the palms and soles may be affected At these areas a nodule forms at the base of a hair, and this remains tense for 2–4 days then becomes fluctuant The covering skin thins and forms a yellow point Rupture occurs and a core of necrotic tissue may be obtained from the center of the boil In chronic recurrent cases there may be reduced resistance of the patient or there may be a staphylococcal strain of in creased virulence The timing of furuncles is intriguing Fre quently a lesion waxes and wanes but a second boil rarely appears until the first is almost absorbed Pain varies in amount but is most marked when the skin is bound down to the underlying tissue, as in the nose or in the outer ear

I have found that some patients who do not carry their own phage type in their noses have received it from a spouse who is an asymptomatic carrier Others carry it in the groin and tend to

have most of their boils on the legs. It is important to question the patient regarding his family contacts A spouse or a child may frequently have had boils carbuncles styes or other obvious staphylococcal infections. Such a round of infections often passes from person to person within a family over a period of years In this situation the whole family needs treatment

TREATMENT —This is discussed later under Sycosis Barbae

CARBUNCLES

These abscesses are boils on a larger scale with several hair follicles involved The necrotic process proceeds deeper in the skin so that multiple areas of discharging pus may develop Because of the larger number of organisms present and the greater tissue death, many of these patients have a constitutional reaction with fever malaise and an elevated white cell count These constitutional symptoms may precede the appearance of a large area of infection Carbuncles occur most often on the nape of the neck or on the back Carbuncles of the neck in males and of the face in females are the most serious

TREATMENT —This is discussed under Sycosis Barbae

SYCOSIS BARBAE

This is a folliculitis confined to the beard area it is similar to a furuncle It is commoner in bearded men than in shaven men A perifollicular erythema leads on to later pustules Sycosis barbae is frequently concurrent with seborrhea Impetigo may precede or follow the attack The source of the organisms is again the patient s nose

TREATMENT —This is similar for the three preceding conditions An area of carriage in the patient (nose axilla or groin) or in his spouse must be found and treated This is best done with the help of phage typing but the heavy growth of a coagulase positive *Staphylococcus aureus* obtained from the area usually

leaves little doubt Bacitracin ointment applied twice daily to the carriage area for 10 days is particularly useful A follow up swabbing 10 days later will detect any failure of treatment.

Patients with fever, leukocytosis or severe spreading cellulitis should be treated systemically for 10 days with an appropriate agent Asymptomatic carriers in the family should receive local treatment only but members of the family with infections and a systemic upset need general antibiotic treatment. In resistant skin sepsis an autogenous vaccine may help

A simple explanation to the patient of the mode of spread of these infections is often beneficial

PARONYCHIA

BACTERIOLOGY —The majority of the cases are due to *Staphylococcus aureus* Occasionally secondary infection with a streptococcus is found Rarely the disease is due to E coli or a proteus

CLINICAL FEATURES —Some part of the nail margin becomes red tender and swollen This area gradually points and sepsis may spread under the nail Lymphangitis and lymphadenitis are not usually found Septic arthritis may develop from a too extensive therapeutic reflection of the nail fold

Occasional cases of chronic paronychia are seen where multiple fingers are affected and when the history extends over weeks or months Deformity of the nail is commonly seen and this may assist in making the diagnosis

TREATMENT —If a small localized area of pus is present and is unruptured, a small incision along the nail fold may be adequate All the pus must be located the nail should be raised but not removed Prior to operation 600 000 units of crystalline and 600 000 units of procaine penicillin are recommended and procaine penicillin should be continued for 7 days Other antibiotics should be substituted if indicated by in vitro tests For larger lesions two lateral incisions should be continued down the lateral margin of the nail on either side A very small gauze drain can be

left in for a couple of days. If pus is present under the nail, only the proximal one third or one half of the nail should be removed

In chronic paronychia the base of all affected nails and all macerated tags of cuticle should be removed at one operation This should be followed by daily treatment with Castellani s paint. In some cases with an urticarial element, aqueous gentian violet irritates less and stains less Ammoniated mercury ointment is also useful (1–3%)

PROGNOSIS —A period of 5–8 days of incapacity occurs with single paronychia. Following an operation all cases heal within 2 weeks a course of more than 1 week being rare

PYODERMA GANGRAENOSUM

This superficial type of ulceration with a markedly under mined border showing a tendency to extend into large ulcerated plaques has various names of which pyoderma gangraenosum is the most common It is frequently associated with other systemic diseases such as ulcerative colitis or chronic empyema. The ulcer may be surrounded by an erythematous area and be crusted over the base however is clean and granulating The margins are serpiginous at the spreading edge but the central area may show some healing There is usually a constitutional reaction with malaise fever and leukocytosis

TREATMENT —This is a serious condition and requires active systemic chemotherapy with an effective drug Gamma globulin may be beneficial if electrophoresis shows a deficiency of this ele ment of the blood proteins

SURGICAL WOUND INFECTIONS

Postoperative infection may vary from 2–3% to 30% or more of the wounds in different wards different centers and from time to time according to the number of carriers among the staff and the amount of unisolated staphylococcal disease on the ward

When many serious infections occur, they are usually of one bacteriophage type

TREATMENT —In the absence of a systemic reaction, drainage is the main method of treatment Stitches and other foreign bodies should be removed and adequate drainage provided When a systemic reaction occurs, antibiotic treatment as outlined in Chapter 9 should be carried out

STAPHYLOCOCCAL BEDSORES

PATHOLOGY —Evenly distributed pressure is well tolerated by the skin but point pressure is not Probably the first changes occur in the pressure susceptible underlying muscle rather than in the relatively resistant skin The greatest points of pressure in bed ridden patients arise over the heels and the sacrum Length of pressure is more important than degree of pressure Poor arterial blood supply predisposes to pressure damage Areas of exudation and increased capillary permeability result in centers ideally suited for bacterial growth Vasomotor rather than neurotrophic changes are the main factors in establishing bedsores although decubiti are common in patients with neurological disorders Pressure alone however does not appear to be a sufficient determinant, as many patients lie in bed for many years without developing bedsores Infection is therefore, an important consideration Skin soaked in body discharges is likely to become infected

BACTERIOLOGY —The pus from bedsores on culture yields staphylococci, pseudomonas or proteus organisms

TREATMENT —Redistribution of pressure by frequent posture change cotton doughnuts, or a mattress with alternating areas of pressure is beneficial A dry skin produced by efficient nursing helps prevent bedsores Active massage and caked talcum powder may damage fragile epithelium and should not be used Magnesium carbonate does not cake A bland ointment carefully applied on abraded areas with aseptic technique and without rubbing is helpful Soap cleansing should be avoided Severely infected areas

can be cleaned initially with Dakin's solution or with digestive enzymes. Systemic and local antibiotics should rarely be necessary

SKIN TESTING

Type specific immunologically active carbohydrates can be isolated from staphylococci. A skin reaction to staphylococcal carbohydrates is rare in infants but is found with increasing frequency as adult life progresses. Type A carbohydrate can be isolated from pathogenic staphylococci, and practically all the skin sensitivity that is seen is caused by this carbohydrate. Type B carbohydrate is found in nonpathogenic staphylococci and a skin reaction to it is rare. There is no correlation between the intensity of the reaction and the presence of antibody or the severity of the disease in patients. It is confusing to find that many apparently normal people have positive skin tests. There is at present no practical use for the skin test

NEONATAL MASTITIS

Although neonatal staphylococcal infection is common involvement of the mammary gland is rare. Mastitis in the newborn is most often hormonal in type

BACTERIOLOGY —All infective cases described have been due to *Staphylococcus aureus*

PREDISPOSING FACTORS —If many staphylococcus carriers are present in the nursery there may be a high incidence of mastitis in the mothers and in the children. If oil is used to bathe the children it may be contaminated with the same organism

CLINICAL FEATURES —Mastitis usually occurs on the eighth to tenth day of life and girls are more frequently affected by it than boys. The breasts first show a marked erythema with induration. The lesion is deep and has the appearance and course of a furuncle. Despite antibiotics abscess frequently develops and an incision is required

TREATMENT —Antibiotic treatment may be necessary if a systemic reaction is present Incision and drainage are necessary in the presence of an abscess

PROGNOSIS —A considerable amount of destruction takes place in the tissues of the affected breast A functional mastectomy has been reported and the breast will be useless for breast feeding in adult life

MASTITIS IN WOMEN

PATHOLOGY —The tissues are hyperemic A single or several lobules are involved first with cellulitis then focal necrosis, hemorrhage and abscess formation Fibrin red cells pus and staphylococci are seen microscopically

BACTERIOLOGY —The organism is almost without exception *Staphylococcus aureus* Rarely streptococci are found they are considered to be secondary invaders In 90% of the cases that are delivered in the hospital and in 70% of those delivered at home the offending staphylococcus is resistant to penicillin It appears likely that the breast is infected from the child who first received the infection from the attending nurse or physician The staphylococcus disappears from the milk at the time that visible pus disappears

INCIDENCE —From ¼ to 14% of all women delivered in the hospital may develop this infection An average figure is 5% and this is a higher rate than occurs in women delivered at home Year to year the incidence is constant So far no evidence of an increased incidence has been described

PREDISPOSING FACTORS —The disease is common in primipara and mothers with female children It is believed that girl babies take less breast milk than boys within the first day or two of suckling

CLINICAL FEATURES —Mastitis has usually been described in puerperal women However in one series of 100 consecutive cases 32% were not related to childbirth Two types of mastitis occur,

superficial and intramammary The ratio of these cases is about 1 4 The infection usually takes place during the second 10-day period following delivery Frequently this disease does not manifest itself until after the mother has left the hospital The time of weaning is also a time of vulnerability due to the reduction in the flow of milk. Presumably tension leads to ischemia and thus to a suitable nidus for bacterial growth

Superficial mastitis—In this type the nursing mother complains of pain and a lump in the breast A superficial inflammation is evident but usually there is no rise in temperature

Intramammary mastitis—In this type there is pain in the breast a lump with a flushing heat and tenderness of the overlying skin The patient has pyrexia and leukocytosis

PROPHYLAXIS —This is dealt with elsewhere under the general heading of the control of staphylococcal infection in hospital Nursing in where each mother takes care of her own infant has helped to cut down the incidence of staphylococcal infections in both the mother and the child

TREATMENT —It is most important to begin early The breasts must be emptied—manual expression being preferred to the use of a pump Frequent and complete emptying is essential

Antibiotics or surgery Only about 25% of intramammary abscesses treated with antibiotics resolve without incision Should the wrong antibiotic be used prolongation of the disease may occur The treatment of penicillin resistant mastitis with penicillin will lead to an increased length of disease and an increased number of incisions for drainage In addition antibiotic treatment may lead to a large amount of granulation tissue which will bleed excessively on incision of the abscess A hard indurated mass may arise after prolonged drug treatment and lead to the suspicion of carcinoma In established abscess antibiotics can only be considered to be ancillary to surgical treatment but in superficial mastitis antibiotics are the main form of treatment

The antibiotic used must be chosen from the general experience in the hospital its effectiveness being confirmed by in vitro

sensitivities It should be continued in full dosage for 10–14 days. When an abscess has already formed, early effective drainage is the surest way of obtaining early healing Exploration with a needle under local or general anesthesia can be carried out if there is doubt, and an incision can be made, if pus is found Treatment by aspiration alone is not effective The incision may be a 1 cm radial incision a 1 cm incision along the areolar margin or if there is infection of the axillary tail of the breast, a 1 cm. tenotomy type incision These small incisions produce a better cosmetic result than the older long radial type of incision A drain or packing is needed for the first few days

Lactation is preferred to suppression of lactation by stilbestrol, but if a lump is present and has not decreased in size by the third day of antibiotic treatment, stilbestrol should be used It can be given in 5 mg doses 3 times a day for 3 days twice a day for 3 days once a day for 3 days then 1 mg 3 times a day for 2 days twice a day for 2 days and once a day for 3 days

PROGNOSIS —Uncomplicated superficial mastitis usually heals in days rather than weeks and it leaves no residual mass Disability from breast abscess usually lasts from 1 week to 2–3 months The condition may recur about 1 month after the original attack The destruction of the breast tissue may lead to an increased susceptibility during subsequent pregnancies Rarely scarring may lead to an inability to breast feed

There is no evidence that any harm occurs to the child by drinking the milk from an infected breast

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3 / RESPIRATORY INFECTIONS

MANY PEOPLE carry potentially pathogenic staphylococci in their noses, but relatively few people develop serious disease of the upper or lower respiratory tract because of these organisms The exact mechanism of natural resistance to the staphylococcus is not fully understood but mucus and the cilia of the respiratory tract form part of this protection In the very young and in the old this protection may be deficient, and in otherwise healthy adults it may be impaired by infection with the influenza virus

SINUSITIS

PATHOLOGY —Inflammation and edema of the mucosal lining of the sinuses lead to blockage of the ostia and the accumulation of pus The lining epithelium may become squamous in type the underlying tissues fibrosed and the periosteum thickened Inflamed reduplications of the nasal mucosa sometimes form polyps

INCIDENCE —This is a very common infection of adults but no exact figures of incidence are available

BACTERIOLOGY —The organisms found in order of frequency are pneumococcus streptococcus staphylococcus, hemophilus and Klebsiella

PREDISPOSING FACTORS —Perennial allergic rhinitis is frequently complicated by sinusitis as is intrinsic asthma Blockage of the nose due to septal deviation or foreign bodies may also predispose Many attacks follow swimming or diving

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BACTERIOLOGY—*Staphylococcus aureus* may be obtained in pure or predominant culture from laryngeal, postnasal or throat swabs in about 90% of cases The culture of lung tissue juice obtained by thoracic puncture has been used for diagnosis No ill effects have followed this procedure After preparing the skin with either iodine or alcohol a dry sterile 16-gauge or 18 gauge needle attached to a 5 ml syringe is inserted into the affected area. If no exudate is obtained from the pleural cavity the needle is advanced a further centimeter or two Suction on the syringe is maintained during both insertion and withdrawal If visible exudate is seen in the syringe it is inoculated directly onto blood agar or chocolate agar plates If no exudate is seen the needle is inserted into a bottle containing 5 ml of glucose broth which is sucked up into the barrel of the syringe and discharged back into the bottle After incubation overnight the broth is subcultured onto the solid media

A small minority of patients have positive blood cultures

CLINICAL PICTURE—More than three fourths of the children who have this disease are less than 12 months old and one half are less than 6 months old Typically at the age of about 12–14 days the infant develops a discharge from the nose usually de scribed as the snuffles a cold or a running nose He becomes irritable and feeds poorly Dyspnea quite frequently interferes with feeding In a day or two the child suddenly becomes pale with a gray tinged cyanosis and is tachypneic with a distressing cough and grunting respirations Fever is in the range of 101–103 F Thick yellow sputum production is common but the infant may swallow it A sample of this for culture may be ob tained by provoking a coughing spasm with a spatula Coughing spasms may be very severe and cause cough syncope The liver may be enlarged and occasionally convulsions or abdominal dis- tention are seen

In fatal cases collapse takes place 24–36 hours before death Cyanosis is marked and the temperature often becomes subnor mal In institutional outbreaks it is common for the early cases

period is necessary to allow diffusion of the antibiotic into the cavities In the early stages careful use of 1–2% aqueous ephedrine nose drops helps to open the ostia and allow drainage of pus

PROGNOSIS —Most of the serious complications such as osteomyelitis orbital abscess cavernous sinus thrombosis meningitis or brain abscess can now be prevented by careful use of medical and surgical treatment. While acute sinusitis usually responds to the treatment outlined many cases of chronic sinusitis relapse

STAPHYLOCOCCAL PNEUMONIA IN INFANCY

PATHOLOGY —Pneumonia is associated with an extra pulmonary staphylococcal infection, such as otitis media, pyoderma and subcutaneous abscesses in one third to one half of the cases On examination of the chest empyema or pyopneumothorax are found to be common complications The pus of empyema is green, yellow or creamy and may have solid flecks Patients with a long history may have adhesions with loculation of the pus

The lungs show areas of consolidation and abscess formation which may be on one or both sides The size of the abscesses correlates directly with the duration of the disease Segments of lung are involved suggesting that the beginning of the process is affected by position The pneumonia tends to be bronchial rather than lobar becoming confluent early The lungs have a gray yellow look with areas of brown or red hemorrhage Pus can be expressed from the yellowish surfaces In the purulent necrotizing, hemorrhagic inflammation there are many thrombosed blood vessels On microscopic examination the bronchioles in the affected pulmonary tissue are generally seen to be filled with polymorphonuclear leukocytes The mucosa for the most part is intact Masses of cocci are often found in the centers of the areas of change There are many microscopic abscesses whose walls are formed by collapsed alveoli containing abundant fibrin strands and occasionally growing fibroblasts About one quarter of the cases have pericarditis





F G 4 (*ab*) —Lu g nfiltrates d ring the fi st few days of illness
FIG 5 (*below*) —Evacuat d abscess s at the bases of both lungs at the height of th illness
(R prod c d by p rmi on of the Editor The Journal of the Iowa State Med c l Society)

to be the *most severe* Frequently pneumonia is associated with but *not necessarily the result of*, a breast abscess in the mother

Coarse crepitations and rales with reduced breath sounds are a constant finding at a later stage Only when the pneumonia is established will there be obvious signs of either consolidation or fluid in the chest It is not possible to differentiate staphylococcal bronchopneumonia from any other kind of bronchopneumonia on physical examination

RADIOLOGY (Figs 4–6) —Initial chest x rays can be normal The characteristic x ray findings of primary staphylococcal pneumonia are an infiltration with circumscribed areas of increased translucency and pleural effusion frequently with an encapsulated pneumothorax Early in the disease, before the formation of abscess small patches of consolidation may be seen These will not be obvious on fluoroscopy and a chest x ray is necessary A tension pneumothorax is sometimes present and may be a danger to life Pneumatoceles in an area of consolidated lung emphysema diffuse or localized and a spontaneous tension pneumothorax with or without empyema are extremely suggestive of staphylococcal pneumonia The x ray findings often change rapidly The pneumatoceles, however persist as long as 3 months Pneumatoceles are typical of suppurative staphylococcal pneumonia but in the absence of a previous history they may be confused with congenital cysts of the lung Areas of localized pleuritis may be shown by a thickened pleural edge or by a diffuse ground glass opacity Films taken in the erect position are especially important to facilitate early recognition of pyopneumothorax Nearly 50% of children under 2 years of age have staphylococcal pneumonia when they show radiographic evidence of pneumonia In children who survive the infection, the x ray picture returns to normal

LABORATORY DIAGNOSIS —It is recommended that 2–3 samples of sputum be cultured by routine means and also examined for fungi One or two blood cultures are advised as pneumonia complicating septicemia has a different progression and treatment from pneumonia occurring alone

occur in the first month A low white cell count is a bad prognostic sign The prognosis of the empyema when treated without antibiotics has been shown to be dependent upon the age of the patient, being worst in the youngest The overall mortality of untreated staphylococcal pneumonia is from 40–70% Surgical measures are extremely important in lowering the mortality With careful surgical treatment the mortality even without antibiotic drugs may be as low as 35% With adequate chemotherapy the mortality is still in the region of 20% In children under 4 months of age however there is a mortality of approximately 50% The prognosis for the restoration of lung tissue is good even when large cavities are present Chronic lung abscesses are rare Some children due to the dyspnea at a period when the bones are soft will show a splaying of the lower ribs The prognosis in children with fibrocystic disease of the pancreas is worse than in normal children

PROPHYLAXIS —Any outbreak of minor staphylococcal skin infections in a newborn nursery must be considered a grave occurrence and the cause of this should be tracked down and dealt with promptly to avoid the development of more serious diseases Aseptic procedures are particularly necessary for all intubation procedures in children less than 1 year old

TREATMENT —In the presence of empyema adequate antimicrobials based on sensitivity tests will not be enough It is imperative to drain the empyema This requires the immediate institution of tube drainage or suction if necessary There is no place for the use of repeated aspiration and no justification for delay in instituting early surgical treatment. Catheter drainage for 2–3 days is recommended The proper equipment must be on hand in the patient s room at all times to meet the possible emergency of a tension pneumothorax The need for immediate and adequate drainage is shown by the fact that in one series of 9 cases treated by aspiration all died whereas in 14 cases receiving intracostal drainage there was a 24% mortality and in 12 cases treated with rubber tube suction drainage there were no deaths

Diagnosis depends upon obtaining a pure culture of *Staphylococcus aureus* or in a very few cases of *Staphylococcus albus*. Alternatively *Staphylococcus aureus* may be the predominant organism in sputum or empyema fluid. Diagnosis may be made

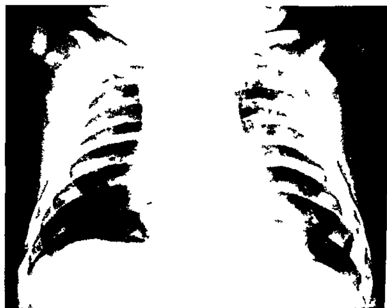


Fig 6—Restoration of normal x ray appearance after convalescence (Reproduced by permission of the Editor The Journal of the Iowa State Medical Society)

on the same basis at autopsy. There are no known serological tests which are of value. At the present lung puncture is not recommended.

A rise in white cell count with a shift to the left is characteristic *but this may be absent*.

Prognosis—In successfully treated cases the time spent in the hospital is from 6 weeks to 2 months. Fever lasts for about 2 weeks and cysts take from 1–2 months to heal. Deaths usually

lung infection and it is most severe in the first 2 years of life

BACTERIOLOGY —*Staphylococcus aureus* is the predominant pathogen but after chemotherapy it may be replaced by *Pseudomonas aeruginosa* or *Proteus vulgaris* It is of interest to remember the increased sodium chloride in the secretions of patients with mucoviscidosis and the ability of staphylococci to grow in the presence of high concentrations of this chemical Staphylococcal infections are uncommon in other parts of the body

PREDISPOSING FACTORS —Measles pertussis and influenza may light up staphylococcal infection in the lungs. It is probable that hospitalization facilitates the colonization of the nasopharynx and lung with staphylococci

CLINICAL FEATURES —Most patients with this disease can be diagnosed by the age of 3 months Despite an increased appetite the child gains weight slowly Bulky foamy foul smelling feces are noted Many children develop a cough with plentiful sputum and dyspnea The cough may be paroxysmal All the symptoms and signs of bronchopneumonia may be present and bouts of infection may recur with increasing severity Progression of the lung disease occurs over weeks or years In chronic cases severe emphysema with a barrel chest may develop and this is followed by cor pulmonale Clubbing of fingers and toes is marked As in many chronic lung infections chronic sinusitis is often found and must be considered in treatment

LABORATORY DIAGNOSIS —Cystic fibrosis of the pancreas can be diagnosed when on duodenal assay pancreatic enzymes (particularly the tryptic activity) are absent and when there is an increase in sweat chloride and sodium concentrations Leukocytosis is present in the children with lung infection

RADIOLOGY —Patchy bronchopneumonia and atelectasis on x ray may be more extensive than was expected on physical examination A combination of emphysema and segmental atelectasis is very suggestive of the disease Lung abscess may develop The heart shadow is narrowed and the diaphragms are flattened

TREATMENT —Antibiotic treatment of the complicating staph

Intrapleural bacitracin has been used in a total dosage of 5 10 000 units given once to twice daily from 2–8 days Adequate oxygen therapy is necessary for the cyanosed infants and the use of a tent is recommended On empirical grounds, one would recommend the use of breast milk obtained by breast pump and given by bottle, rather than a cow s-milk formula The child should be under strict respiratory isolation as this is a very good focus for the occurrence of other cases The use of antibiotics is discussed in Chapter 9 Erythromycin cannot be recommended as a routine drug at the present time, novobiocin or chloramphenicol are the drugs of choice before sensitivities are known The course of antibiotic treatment should cover a period of at least 6 weeks The temperature can be expected to fall only after a week or more of treatment A very difficult question—whether to discharge the child from the hospital or not—arises when there are large cysts present in a child who is otherwise well Probably it would be safe to end the child home after 3 weeks have passed from the onset of clinical recovery There is then little danger of the development of pneumothorax

LUNG INFECTIONS IN PATIENTS WITH CYSTIC FIBROSIS OF THE PANCREAS

SYNONYM —Mucoviscidosis

Children with mucoviscidosis may have their disease diagnosed first following an attack of lung infection

PATHOLOGY —The secretions of the bronchial tree become plentiful and sticky so that obstruction of the bronchi by these secretions plays a large part in the lung pathology Inflammation occurs in and around the bronchioles This chronic low grade inflammation leads to edema infiltration and later fibrosis of the smaller bronchi and the obstruction leads to hypertrophy of the muscularis Bronchopneumonia and atelectasis occur A few patients develop bronchiectasis or right ventricular hypertrophy or both late in the disease

INCIDENCE —Most of the children with this disease develop

lung infection and it is most severe in the first 2 years of life

BACTERIOLOGY —*Staphylococcus aureus* is the predominant pathogen but after chemotherapy it may be replaced by *Pseudomonas aeruginosa* or *Proteus vulgaris* It is of interest to remember the increased sodium chloride in the secretions of patients with mucoviscidosis and the ability of staphylococci to grow in the presence of high concentrations of this chemical Staphylococcal infections are uncommon in other parts of the body

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ylococcal lung infection has prolonged life The laboratory assessment of the sensitivities of the staphylococcus isolated from the sputum is helpful in making a choice of the drug for systemic treatment Many children have been maintained on chemotherapy for months or years. Frequently it has been noted that the strain of staphylococcus isolated from the sputum becomes resistant to the drug being used, but the child continues to do well In such a situation the clinical response of the patient has to be the guide to treatment Tetracycline, 5–10 mg /lb daily, has been used but erythromycin in similar dosage is preferred by some Novobiocin due to rash producing effects is not recommended Inhalation therapy with antibiotics such as neomycin has been beneficial In severe cases resistant to the usual forms of treatment intravenous vancomycin or ristocetin may help

In some children small areas of atelectasis have been cleared by the use of a coughing machine Enzymes and detergents usually have not been of help In a few selected cases where a localized area of atelectasis has been present for several months a lobectomy has been good treatment.

It is best to keep the children out of bed for as long as possible

Prognosis —Suppurative bronchitis is still the major cause of death in cystic fibrosis of the pancreas Frequently this is due to organisms which are highly resistant to antibiotics Many deaths occur in the 3–5 age group The average length of lung disease is about 3 years The prognosis is worse when extensive segmental atelectasis is present If the patient reaches adolescence there is usually no progression of the lung disease

PRIMARY STAPHYLOCOCCAL PNEUMONIA IN ADULTS

The literature on those cases of pneumonia which do *not* follow influenza is comparatively scanty Only recently has it been appreciated that staphylococcal pneumonia is a common terminal event in many patients debilitated from other causes

Pathology —In this type of pneumonia the predominant

finding at autopsy is a diffuse bronchopneumonia which fre quently is described as necrotic and sometimes also hemorrhagic Discrete abscesses are quite uncommon and so is empyema

The histology shows many polymorphs and clumps of Gram positive cocci in affected bronchioles and the alveolar ducts and surrounding alveoli are filled with hemorrhage edema fluid Thrombi are common in the pulmonary vessels Quite often microscopic abscesses are found

INCIDENCE —Most frequently patients are over 60 years old but all age groups can be affected There are 2 or 3 men to every woman with staphylococcal pneumonia

CLINICAL PICTURE —In patients who are younger and rela tively well at onset there is increasing dyspnea pleural pain rigors and a cough The fever is high and remittent and the pulse is relatively slow When staphylococcal bronchopneumonia occurs in debilitated hospital patients who have been admitted for some other disease the onset may be marked by fever cough and dysp nea or mental confusion Sputum production by these patients is not prominent but when it does occur the sputum may be blood tinged Often leukocytosis is absent and the main findings on ex amination are crepitation or rales scattered throughout the lungs Evidence of lobar consolidation is uncommon but scattered areas of impaired air entry occur Despite intensive treatment these patients frequently go downhill rapidly developing cyanosis and later shock In many ways they resemble the patients who have concurrent influenzal infection along with staphylococcal pneu monia and it has been postulated that there might be a predis posing factor common to both of them perhaps pulmonary edema which is common in debilitated hospital patients

LABORATORY DIAGNOSIS —This depends on the predominance of staphylococci in the sputum

RADIOLOGY —It is uncommon to see cavities in the x rays of these patients If they do occur they are usually temporary Pleural effusions occur but they are less common than in chil dren Pulmonary infiltration is the only finding that is constant

Occasionally the hilar glands are observed to be enlarged

PROGNOSIS —The outlook is extremely grave Quite frequently the diagnosis is only made at autopsy The fatality rate is about 80% In one series staphylococcal pneumonia made up 3% of all pneumonia cases admitted to hospital, and in another it constituted 20% of all the pneumonias seen In those who recover there may be residual pulmonary fibrosis which contrasts with the disease in young children where complete resolution is the rule

TREATMENT —If pulmonary edema is a factor in the susceptibility of debilitated patients any fluid therapy has to be used very carefully The main treatment is to give an antibiotic which may be expected to deal with the staphylococci currently present in the hospital and as soon as possible to substitute for this the appropriate antibiotic as indicated by *in vitro* sensitivity tests

LUNG ABSCESSES DUE TO STAPHYLOCOCCI

PATHOLOGY —Abscesses are most often found at the periphery of the lung under the pleura They are bronchogenic in origin starting as an inhalation bronchopneumonia of infected secretions In the less common pyemic type the abscesses are small multiple and bilateral

INCIDENCE —These cases make up about 10% of all lung abscesses About 20% of the patients are infants There is a 2 1 preponderance of males Usually staphylococcal abscesses do not follow foreign body inhalation accidents or abdominal operations as is the case with other types of lung abscess

PREDISPOSING FACTORS —In about 20% of cases these abscesses are seen in patients with emphysema chronic bronchitis or asthma About 10% of lung abscesses follow attacks of influenza

CLINICAL FEATURES —The patient is frequently prostrated with an illness of insidious onset The temperature is about 104–105° F with a relatively slow pulse Generalized sweats are very common A high pulse rate may indicate a complication such as

pericarditis pneumothorax or a large pleural effusion An abscess can form in 5 days or it may form as a late after-event of an apparently healed septicemia. Small amounts of blood stained or bloody purulent sputum are brought up and this is very similar to pus from a staphylococcal skin abscess Occasionally the diagnosis is made on routine chest x ray in a patient with malaise and other nonspecific complaints In about a quarter of the patients with lung abscess empyema develops and cerebral abscesses can occur

LABORATORY DIAGNOSIS.—The diagnosis depends on the predominance of *Staphylococcus aureus* in the sputum but frequently a pre-emptive diagnosis can be made on a combination of the clinical findings and the x rays A blood culture should always be taken

RADIOLOGY.—Due to the bronchogenic origin and subsequent distention with air a large cavity does not necessarily mean gross lung destruction Cavities resemble a soap bubble and may have a very thin margin In the pyemic type multiple small wooly opacities are soon replaced by small empty cavities

TREATMENT.—The main approach here is conservative and nonsurgical Prolonged antibiotic therapy is recommended the course of the disease being followed by frequent x rays The treatment of a complicating empyema must be surgical

PROGNOSIS.—Before antibiotics were available the mortality in children varied from 25–80% With the careful use of antibiotics deaths should be rare Usually complete resolution takes place and follow up bronchograms are normal In about 10% of cases there is permanent damage usually consisting of minor bronchiectatic changes

POST INFLUENZAL STAPHYLOCOCCAL PNEUMONIA

PATHOLOGY.—At autopsy in the lower half of the trachea there is granulation tissue in place of the normal ciliated epithelium In some cases ulceration is present Lobar pneumonia

frequently with pulmonary edema, is twice as common as bronchopneumonia Dry or wet pleurisy is sometimes found Abscesses are rarely apparent to the naked eye although minute abscesses are frequent Hemorrhage and necrosis in the lung tissue are common In patients dying early there may be very little cellular reaction on microscopic examination There is a protein rich material in many alveoli and blood in others In about two thirds of post influenzal cases cardiomegaly is seen and the myocardium is edematous on histological examination

BACTERIOLOGY —About one half of the fatal cases show *Staphylococcus aureus* in the lungs at autopsy Many different phage types may be involved Next most frequent to staphylococci are pneumococci and nonhemolytic streptococci The findings in the 1957 pandemic contrast with those in the 1918–1920 pandemic when *H influenzae* was much more common It may be in a rare fatal case that no bacteria are found Presumably, in this case the pneumonia is due to the influenza virus

INCIDENCE —Males are three times as commonly affected as females which differs from the equal involvement of the sexes in flu The disease is commonest in the fourth to the seventh decade

PREDISPOSING FACTORS —About two thirds of post influenzal pneumonias have underlying diseases such as bronchitis emphysema or chronic lung disease hypertension or chronic rheumatic heart disease (particularly mitral stenosis) A number of cases have occurred in the last trimester of pregnancy

CLINICAL PICTURE —A pneumonia which is indistinguishable from noninfluenza lobar pneumonia may complicate influenza Immediately after or sometimes 7–10 days after a typical flu illness cough becomes marked there is a vague discomfort in the chest and sometimes dyspnea A rapid pulse rate is common Sputum is not frequent but when present, it is sticky and may be tinged with blood Decreased air entry and scattered rales are the main findings Depending on the extent of the infection rales may be heard widespread throughout the lung

In fulminating cases the onset of dyspnea, a high fever chills

and cyanosis is sudden usually coming after 1–2 days of influ enzal symptoms Shock may supervene and may be associated with disorientation or even coma If any sputum is raised it is frothy and blood stained Severe retrosternal pain may develop There is usually bilateral dullness on percussion with widespread rales A pleural friction rub is occasionally heard Rarely a septi cemia complicates the pneumonia. Death may occur within 2 or 3 days of onset.

Radiology —The x ray picture does not differ from that of pneumonia in noninfluenza periods except that the rate of progression is more rapid

Prevention —Susceptible individuals should be vaccinated against influenza in pandemic periods In the absence of pneu monia influenza is best treated without antibiotics to prevent super infection with resistant staphylococci Confinement at home is preferred to treatment in a hospital In those with an occupa tional exposure to staphylococci such as physicians and nurses it is a mistake to return to work before full recovery from influenza.

Treatment —The fulminating cases are an emergency situa tion where rapid diagnosis and high dosage intravenous chemo therapy are essential Despite apparently adequate chemotherapy some patients die Chloromycetin and novobiocin are the anti biotics of choice at the time of writing If the strain is susceptible to erythromycin this is a valuable drug

Due to the great outpouring of fluid a tracheotomy with endotracheal suction is usually necessary Adrenal steroids may be beneficial Noradrenalin may be necessary to combat shock

The treatment of the nonfulminating cases involves the use of carefully chosen antibiotics for 2 or more weeks

Prognosis —The case fatality of patients admitted to the hos pital with pneumonia exceeds 25% despite antibiotic treatment. Among 1 429 influenza patients in Iran however there were only two deaths this indicates that fatal pneumonia cases although moderately common in a hospital make up a very small portion of the influenza disease picture

EMPYEMA

Empyema in children has already been dealt with. In adults this complication is rare

PATHOLOGY —Thick yellow pus is found compressing the lower part of the lung Frequently there is also hemorrhage

BACTERIOLOGY —*Staphylococcus pyogenes* is usually easily obtained on culture but in a few cases the pus is sterile by the time it is detected

PREDISPOSING FACTORS —Late and inadequate chemotherapy of staphylococcal pneumonia may lead to the development of empyema When postoperative infection occurs after thoracic surgery it is most frequently staphylococcal in nature In rare cases it may follow trauma to the chest

CLINICAL FEATURES —When the patient with pneumonia fails to thrive and physical examination reveals evidence of a small or moderate pleural effusion we know that the pneumonia has been complicated by an empyema The final diagnosis depends on a thoracic paracentesis This should not be delayed

LABORATORY DIAGNOSIS —Patients have a moderate or marked leukocytosis and a mild anemia

RADIOLOGY —Radiology may reveal an empyema where it was not suspected In patients where the diagnosis has already been made radiology helps in planning the thoracentesis

TREATMENT —The pus present in the chest must be removed In an early case repeated aspiration should be carried out with the use of the enzymes streptokinase and streptodornase In some cases local bacitracin is beneficial However in the majority of cases, surgery will be required to provide adequate drainage and to help in the preservation of the underlying lung

PROGNOSIS —With modern treatment deaths should be infrequent In an occasional patient a pericarditis develops and septicemia may follow and later decapsulation of the lung may be necessary to allow the lung to function normally

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4 / OSTEOMYELITIS

PATHOLOGY —Osteomyelitis is an inflammation of the soft parts of bone with secondary effects on the bony casing It is predominantly hematogenous in origin, but the infection is sometimes introduced directly as in a compound fracture or at the time of operation In at least one third of the cases, the primary infection is boils carbuncles or other cutaneous infections

Osteomyelitis is a disease of growing bone, only 3% of cases begin after ossification is complete The infection usually starts in the metaphysis where the blood supply is rich Trauma in this area is common and because of the structure of the end arteries circulating organisms are trapped It is thought by some physicians that at this site phagytosis may be so poor that clearance of circulating organisms is inadequate Acute inflammation will destroy the bone and chronic inflammation leads to bone sclerosis Further necrosis may be caused by septic thrombosis of vessels As infection progresses, it erodes through bone and appears beneath the periosteum In some cases it spreads subperiosteally without eroding the cortex, rupture may occur later with subcutaneous infection and sinus formation Areas of bone lose their blood supply and die sequestra are formed New bone may be laid down by the periosteum in a regular pattern to form an involucrum The upper metaphysis of the humerus all metaphyses of bones at the elbow and both metaphyses of the femur lie partly or wholly within the joint capsule thus osteomyelitis in

these regions may lead to septic arthritis of the neighboring joint.

BACTERIOLOGY.—Hemolytic *Staphylococcus aureus* is the cause of idiopathic hematogenous osteomyelitis in 95% of the cases with 3% caused by streptococci 1% by pneumococci and rarely by such other organisms as coliforms. *Staphylococcus aureus* is the usual cause in iatrogenic osteomyelitis or the osteomyelitis following compound fractures but a variety of other organisms can be the cause

NEONATAL OSTEITIS

This infection is found in infants under 1 month old and may be either benign or severe All cases should be considered severe initially because accurate assessment is very difficult and often must be made retrospectively Soft tissue infections are not common in the newborn and a bony focus must be suspected In all cases whether benign or severe tenderness of the bone is *the* sign to look for Delay in diagnosis may have serious consequences.

In the benign group—53% of total cases—life is not in danger at any time during the course of the disease When the disease is benign we find the *maxilla humerus* and *femur* are involved most often but when the disease is severe several bones especially those near the shoulder and the knee are apt to be involved Swelling with or without skin discoloration is found The child is irritable especially on handling is febrile and has a leukocytosis In some a pseudoparalysis develops because of muscular spasm

Aspiration of pus through a short, large-bore needle is a useful technic for diagnosis This pus can be tested to determine the nature of the organism and also its sensitivities to antibiotics

TREATMENT.—Foreign bodies and loose teeth should be removed where necessary repeated aspirations may be required as part of the treatment antibiotic treatment should continue for at least 3 weeks Otherwise the treatment is as given below for osteomyelitis of older children

PROGNOSIS.—Records show that infants with untreated neo-

natal osteitis have a mortality rate of 60%, while among older children the mortality rate is 22% With effective treatment the mortality rate for infants may be as low as 25% but a large proportion of these infants may be left with one or more abnormal joints In other respects the prognosis corresponds with that of older children

OSTEOMYELITIS OF CHILDREN AND YOUNG ADULTS

Boys between ages 3 and 15 are the most frequently affected by this disease girls have it only one third as often The bones most often affected are the femur (38%) tibia (38%) humerus (14%) radius (4%) fibula (3%) and ulna (3%) One side is as frequently affected as the other Affected children are sometimes debilitated by other illnesses such as the common contagious diseases of childhood Some authors point out that exposure to cold may be a significant preceding event Occasionally outbreaks have occurred in circumstances that suggest the presence of a bone localizing phage type of staphylococcus

CLINICAL FEATURES —After an incubation period of malaise lasting from a few hours to a few days there is an acute onset with chill fever and exquisite tenderness over the bone The child is obviously ill flushed and bright eyed usually he has a furred tongue Localized tenderness occurs over one of the long bones and examination of this area is resented because it causes pain In a few severe cases the temperature may be subnormal At a slightly later stage in the disease swelling develops and edema may be present If the femur is involved the tenderness is usually in the popliteal space If the tibia is involved the tenderness will be found in the upper growing end

The neighboring joint may be distended with fluid from a sympathetic inflammatory reaction With co-operation from the patient, a good range of movement will be present but if the joint is the seat of septic inflammation the range of movement will be greatly restricted Aspiration under general anesthesia may be necessary to make a correct diagnosis

LABORATORY DIAGNOSIS —A leukocytosis is present with an increase in immature polymorphs About 50% of the cases show a positive blood culture if they are seen in the first week.

RADIOLOGY —In the early period of acute cases no abnormalities are found. After 2 weeks or more diffuse osteoporosis is seen in the region of the metaphysis and new bone may outline the raised periosteum. In chronic cases the bone is thickened and shows irregular and patchy sclerosis which has a honeycombed appearance Sequestra appear as dense loose fragments with irregular but sharply demarcated edges

DIFFERENTIAL DIAGNOSIS —Acute rheumatic fever has a more gradual onset. The pain is less acute and demanding and the swelling is more definitely localized in the joint. Many joints are involved in rheumatic fever and the leukocyte count is not so high. In osteomyelitis there is a more serious constitutional disturbance Bacteriological studies of the throat, joint fluids or abscess aspirates will assist in making a definitive diagnosis.

In some children the spread of the disease to the surface may cause it to be confused with erysipelas or cellulitis Occasionally there will be trouble in differentiating osteomyelitis from acute pyogenic arthritis where there is greater spasm of the muscle and more limitation of movement. Effusion into the joint space occurs sooner in pyogenic arthritis than it does in osteomyelitis. Trauma scurvy hemophilia or the crises of sickle cell anemia may occasionally cause difficulty in diagnosis

TREATMENT —In the years immediately following 1935 it was realized that early surgery was inadvisable as mortality rates approximated 35% after operations in the first week whereas when surgery was done in the second week the mortality rate fell to 13% and in the third or subsequent weeks it fell to 10% These mortality rates of course do not apply today but they illustrate the need of waiting for localization or for antibiotic control of the infection Chemotherapy can be started after investigations to establish a diagnosis have been begun or when a bacteriological diagnosis has been made As a rule surgery should not be at

tempted until chemotherapy of the correct kind has been instituted Initially the chemotherapy will be that judged to be most effective in treating the prevalent staphylococci of the district This will be particularly important in the neonatal group, most of whom will have acquired their infection in hospital A number of the older group of children who have acquired their disease at home will have an organism sensitive to the commonly used antibiotics, and careful choice of antibiotic is not so important

Chemotherapy should be continued for a minimum of 3 weeks, or until *after local cultures and blood cultures are sterile* The importance of this is emphasized by two cases in the literature in these a penicillin sensitive staphylococcus was isolated from the bone marrow 28 days and 38 days after the institution of adequate penicillin therapy Blood cultures at 2–3 day intervals are recommended If they are not sterile 3–4 days after the onset of therapy the sensitivity of the organism should be carefully reassessed

The need to delay surgery is less obvious in the era of chemotherapy than it used to be The more radical forms of surgery are, however seldom necessary After aspiration of pus through a wide bore needle for diagnostic purposes surgery must be directed *toward relieving the pressure and toward draining the pus* Simple incision may be adequate, but remember that, if the case has lasted for more than 24–48 hours the medulla of the bone is probably involved In these cases either bone drilling or actual removal of small pieces of cortical bone may be necessary to give adequate drainage Recovery without surgery can be expected in some cases if there is a rapid response to chemotherapy but persistent symptoms and localizing signs lasting for more than 48 hours are an indication for surgery

In the treatment of chronic or recurrent osteomyelitis careful x rays should be taken from many different angles If this fails to indicate the position of sequestra, then tomography may be useful If sinuses are present, they should be visualized with lipiodal before operation is contemplated In cases in which there has been chronic suppuration with discharging sinuses for many years

amputation has been considered, but adequate surgical drainage in these cases still yields satisfactory results in a good per cent of cases especially when it is used in conjunction with appropriate chemotherapy Amputation has many problems and is the least desirable solution for these chronic suppurative cases

PROGNOSIS —Untreated patients may spend from 20 to more than 200 days in the hospital with the average stay ranging 80–90 days With modern treatment patients spend an average of 30 days in the *hospital the outside limits being 10–100 days* Response to treatment is best determined by a consideration of the clinical state of the patient, the temperature leukocyte count and the sedimentation rate More than half of the fatal cases die early generally within the first 5 days and usually of disseminated pyemia. Ecchymosis is common in fatal cases Morbidity takes the form of adherent scars at the site of operation Involvement of joints may be followed by ankylosis and is discussed in the following section About 10% of untreated cases develop pathological fractures and 20% have sequestra which require surgical removal Now that we have adequate treatment sinuses are rare Amyloid disease is a historical curiosity that is no longer seen

An important sequela to this type of infection is lengthening of the affected limb often amounting to 1 or 2 cm It has occurred in about half the cases in some series but with more prompt treatment it is declining in frequency The mortality from this disease when untreated has varied in different series from 35 to 55% The rate seems to be higher following infection of the femur than following infection of the tibia and the fibula when other bones are *involved the rate is lower Deaths from osteomyelitis* have become rare with modern treatment

OSTEOMYELITIS OF THE VERTEBRAE

This disease is suggested by localized pain in the region of the vertebrae following a pre existing septic focus elsewhere The onset is relatively rapid with fever and leukocytosis

OSTEOMYELITIS OF LUMBAR VERTEBRAE FOLLOWING URINARY INFECTIONS —There is a connection between the prostatic plexus of veins and the veins of the vertebra This can be demonstrated by the injection of radiopaque material into the dorsal vein of the penis and the appearance of the dye in the region of the lumbar vertebra

Septic spondylitis affects the lumbar vertebra in 54 6% of cases the dorsal vertebra in 25 9% cervical in 10 3%, sacral in 17 6% and coccygeal vertebra in 1 6% of cases Cord compression from spinal epidural abscess may occur

BACTERIOLOGY —The causative organism is the staphylococcus in 72% of cases the streptococcus in 15% the pneumococcus in 3% and a mixed infection in 8% Other organisms are rarely causative

RADIOLOGY —The first signs of damage are rarefaction and loss of trabecular detail of the bone This leads to a fuzziness along the upper and lower bony plates of the vertebra With more severe damage partial or complete collapse will occur In some cases an early sign is the narrowing of the intervertebral disc Occasionally subligamentous new bone formation is seen

DIAGNOSIS —This is now easily done by radiology and by needle biopsy By the latter means, the exact bacteriological diag nosis and the sensitivities of the organism can be determined In certain centers the diagnosis is now made by an anterior approach to the vertebral bodies by a transcervical transpleural or retro peritoneal route

TREATMENT —This is treated with specific chemotherapy plus support to the vertebrae from plaster, a brace or a corset Spon taneous fusion usually makes operative fusion unnecessary

SEPTIC ARTHRITIS

PATHOLOGY —In general this is confined to one joint The route of infection may be via the blood as in acute osteomyelitis,

or it may be a direct puncture injury Recently septic arthritis due to staphylococci has been seen as a complication of steroid ther apy The exudate in the joint may be serous sanguineous or puru lent in type

BACTERIOLOGY —Septic arthritis is very often caused by cocci the staphylococci being the most frequent Others are gonococci pneumococci hemolytic streptococci and meningococci and oc casionally other bacteria

CLINICAL FINDINGS —In the less severe cases the symptoms re semble those of acute rheumatism Movement of the joint actively or passively is almost impossible There is severe pain swelling and stiffness The patient may complain of severe pain on drop-ping off to sleep at night as the muscular guarding of the joint relaxes There is usually a high temperature with a high leukocyte count

LABORATORY DIAGNOSIS —The joint hould be aspirated for diagnostic purposes and any fluid withdrawn should be submitted to histological and bacteriological examination There should be an x ray examination to rule out the concurrent presence of osteo-myelitis or the presence of a foreign body When the joint fluid shows a cell count of more than 11 000 leukocytes per cc (60% or more of these being polymorphs) the cause of the effusion is usually bacterial Those fluids with less than 5 000 leukocytes per cc and fewer than 50% polymorphs are likely to be sterile on culture

TREATMENT —The joints should be repeatedly aspirated Peni cillin or neomycin may be instilled in the joint in place of the re moved fluid Most of the other antibiotics are too irritating to be used for this purpose Concurrent systemic therapy should be given

ASPIRATION OF JOINTS —To enter the *hip joint* a needle is inserted at a point 2 inches below the anterior inferior iliac spine and pushed upward backward and medially or it is inserted from the side above the upper border of the great trochanter going inwards and slightly upwards following the line of the fem

oral neck To aspirate the *knee joint* the patella is pulled away from the operator and the needle is passed obliquely between the femur and the patella with the quadriceps muscle relaxed With the knee flexed 90° the joint can be approached through the center of the patellar tendon The needle is parallel to the long axis of the femur and penetrates the ligament to a depth of 1½-2 inches An anterior approach is made to the *ankle joint* between the lateral border of the peroneus tertius and the lateral malleolus or between the medial border of the tibialus anterior and the medial malleolus using a backward and slightly downward movement A posterior approach can be made between the tendo calcaneus and the peroneal muscles The *shoulder joint* is entered in the delto pectoral angle directly through the anterior part of the capsule or between the acromion process and the head of the humerus with a downward and backward movement The *elbow joint* is entered from behind immediately above the olecranon between the epicondyles with the elbow flexed at about 135°, or at the lateral site of the olecranon with the elbow at a right angle The *wrist joint* is aspirated from the posterior aspect immediately below the lower end of the radius between the extensor indicis and the extensor pollicus longus

PROGNOSIS —The functional prognosis is better following aspiration than after open drainage The poorest results are obtained on patients between the ages of 6 and 18 The death rate is low

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5 / GASTROINTESTINAL SYSTEM AND ABDOMEN

THE LIVER *and the spleen have excellent natural protection* against staphylococci, whereas the kidney is frequently the site of abscess formation It is possible that the amount of reticulo endothelial tissue in these organs explains their difference in sus ceptibility to the staphylococcus

Direct invasion of the bowel by staphylococci is rare Often what has happened is that the natural enteric flora has been re duced by artificial means such as the use of broad spectrum anti biotics Many times we consider that the ubiquitous coliform organisms are merely excretory products but they may have a protective function and inhibit or destroy staphylococci The natural resistance of the bowel may also be overcome by a large dose of preformed staphylococcal enterotoxin

ACUTE SUPPURATIVE PAROTITIS

PATHOLOGY —With this disease the organism enters the gland through the parotid duct

BACTERIOLOGY —In most cases, a coagulase positive *Staphylo coccus aureus* can be grown from the material expressed from the parotid duct Occasionally a blood culture also shows a growth of *Staphylococcus aureus* Mixed cultures are uncommon but at times another organism such as a *Hemophilus influen ae* is found *in* pure culture

INCIDENCE —Suppurative parotitis occurs most often in pa

tients over 50 who are debilitated from some other disease or, frequently from an operation Cases in young otherwise healthy adults are in the minority and only occasionally is the disease seen in newborn infants. It affects slightly more males than fe males The yearly incidence appears constant and no evidence of a seasonal change has been noted

Predisposing factors —Genito-urinary or gynecological operations often predispose to parotitis and it often appears after nasal tracheal or stomach tubes have been used. Prolonged peri ods of hospital treatment offer an opportunity for picking up the epidemic strain of staphylococcus Many of the affected patients have poor oral hygiene, and others have noted that poor renal function is present also but this has not been our experience

Clinical features —In acute suppurative parotitis there is a rapid onset of swelling occasionally accompanied by pain Usu ally one gland is involved but in 25% of cases the condition in volves both glands, and once in a while it will result in trismus or temporomandibular joint pain On examination the gland is *obviously* swollen and palpation causes pus to be expressed from the parotid duct Induration of the gland is uncommon as is a redness over the gland The majority of patients have an eleva tion of temperature which seldom exceeds 102 F at times the disease occurs without fever Occasionally spontaneous rupture occurs through the skin of the cheek or into the anterior wall of the external auditory meatus

Laboratory diagnosis —This is best done by culture of the parotid duct discharge The white cell count will be found to be moderately elevated Occasionally difficulty with a stone in the parotid duct will arise and this can be clarified by palpation or an x ray

Treatment —This infection is serious and high dosage oral or parenteral therapy is definitely indicated The antibiotic ther apy should be controlled by in vitro sensitivity tests on the organ ism which had been isolated from the pus and the treatment should last for at least 2 weeks to prevent relapse X ray treat

ment has been used in the past, but published records do not suggest that it gives better results than antibiotics do Surgery should not be necessary Iodine to increase the secretion of the gland, hot or cold packs locally, lemon juice chewing gum or hot, saline gargles have been recommended No other treatment however, can replace antibiotic treatment

PROGNOSIS —In the past the mortality was 40–60% in this condition Now with early adequate modern therapy, the mortality should be less than 20%

STAPHYLOCOCCAL FOOD POISONING

PATHOLOGY —This disease is due to the ingestion of preformed staphylococcal enterotoxin Food poisoning is so rarely fatal that there is no information on pathology

BACTERIOLOGY —The causal foods are most often custard filled bakery goods and ham tongue or other cold salted meats (Salt, inhibitory for most bacteria does not interfere with the growth of staphylococci) *These foods may contain up to 100,000 000 staphylococci per gram*

All virulent staphylococci produce coagulase but not all coagulase positive strains produce the enterotoxin responsible for food poisoning All coagulase negative staphylococci tested have failed to produce enterotoxin Both aureus and albus strains can be involved

A careful epidemiological inquiry regarding the food eaten by the patients may lead to the identification of the contaminated food Suspected food should be cultured on blood, eosin methylene blue and Salmonella Shigella agar Stool and vomitus specimens should be cultured on the same media to rule out diarrhea caused by various enteric pathogens *Staphylococci are not usually found in the feces.*

INCIDENCE —The commonest form of food poisoning in the United States is this staphylococcal food poisoning It accounts for 50–80% of those outbreaks where the cause is determined In

Great Britain the figure is much lower, but the proportion of cases caused by staphylococci is rising everywhere

Predisposing factors —Anyone can be susceptible to this disease if he ingests preformed enterotoxin From 70–100% of exposed people are affected

Clinical features —About 2 or 3 hours after eating con taminated food there is malaise and distaste for food After this anorexia salivation nausea vomiting and retching rapidly fol low In severe cases bloody mucus is present in the vomitus and stools and muscle cramps headache and sweating are experi enced In mild cases diarrhea and abdominal discomfort may be the only features People vary in the degree of their susceptibility to the enterotoxin for reasons which are still unknown The rapid onset short duration and usual absence of fever help to dis tinguish this from other infective food poisoning

Laboratory diagnosis —Culture filtrates made from staphy lococci obtained from food suspected of causing an outbreak can be tested in human volunteers monkeys or kittens The latter test is preferred in routine investigations

In human volunteers 25 cc of culture filtrate taken by mouth within 3 hours has caused symptoms which have simulated the disease Small amounts of the culture have caused nausea and mild gastrointestinal distress This method has most frequently been used for research investigations

In monkeys 50 cc of filtrate is given by stomach tube or 1 cc per kg of boiled filtrate is given intravenously After 3 hours vomiting abdominal discomfort and diarrhea occur Most of the animals recover Tests by this method are too expensive for rou tine use

In kittens weighing 350–530 Gm 0 5 ml of potent filtrate intraperitoneally will cause symptoms This test requires careful controls with uninoculated broth When the intravenous or intra peritoneal route is chosen culture filtrates are used that have been treated with 0 3% formalin and then kept at 37 C until α and β hemolysins are no longer detectable

Recent work suggests that enterotoxin may be identified by its infrared spectrum

PREVENTION —Food handlers with staphylococcal infections should be prohibited from working Unfortunately, asymptomatic carriers can also infect food therefore personal cleanliness by food handlers is of great importance Low temperature pasteurization will kill staphylococci that have been accidentally introduced and this is now applied to custard filled puffs and other pastry goods It is unfortunate that the enterotoxin itself is heat stable and will resist boiling Staphylococci can produce enterotoxin in 5 hours or less and, therefore storage at a suitably low temperature is very important with food that is liable to be contaminated

TREATMENT —Most cases are self limiting Some symptomatic improvement may be gained with tincture of opium or kaopectate In severe cases intravenous saline or Ringer's solution may be required

PROGNOSIS —The average case lasts 1–3 days Deaths are extremely rare

POSTANTIBIOTIC STAPHYLOCOCCAL ENTERITIS

PATHOLOGY —The bowel contents are liquid and dark green in color The wall of the bowel is thickened by edema and there is a yellow fibrin like membrane adhering to mildly discolored areas of bowel when the membrane is pulled off, the underlying bowel is hemorrhagic Newly involved areas will show only congestion and edema

Enlarged soft lymph nodes will be found in the mesentery of the large or small intestine In some cases both the large and the small bowels may be affected but usually lesions are chiefly in the large bowel

BACTERIOLOGY —Gram positive cocci can be seen in large numbers in smears made of the stool The stool should be cultured on blood agar for diagnosis, and a heavy growth of staphylococci will

confirm the tentative diagnosis made on direct smear (Care must be taken to differentiate active infection from the fecal carrier state in the latter case direct smears will show only an occasional Gram positive coccus) Staphylococci of the same phage type may be carried by several patients in the ward Enterotoxin has been isolated from filtrates of strains causing this disease

INCIDENCE —There is considerable variation in the incidence of staphylococcal diarrhea in patients treated with oxytetracycline As many as 9 cases among 200 patients have been reported but in general the incidence is much lower The disease is common when high doses of a broad spectrum antibiotic or penicillin streptomycin mixtures are used over a long period The disease however can occur after as little as 4 Gm of oxytetracycline Outbreaks are often seen in hospital wards

Postoperative pseudomembranous enterocolitis and postantibiotic staphylococcal enteritis A disease with all the clinical characteristics of postantibiotic staphylococcal enteritis has been known to occur occasionally after operation In a number of patients with enterocolitis cultures of the stool did not reveal staphylococci *However this is not conclusive because the media used* were usually those normally employed to detect enteric pathogens and these media are inhibitory for staphylococci It is of some interest that sections of the bowel of the first-observed case have been shown to contain masses of Gram positive cocci The two diseases appear to be identical and may be differentiated only by factors leading to the lowered resistance of the bowel to staphylococci

CLINICAL PICTURE —The onset usually occurs 1–6 days after the beginning of the administration of the antibiotics There is abdominal discomfort and bloating and a rise in pulse rate followed later by a rise in temperature The outpouring of fluid into the gut leads to oliguria and then anuria In severe cases the triad of signs is shock fever and oliguria The stools are frequent and fluid often containing blood and mucus Vomiting may be the predominant symptom or in postoperative cases the fluids sucked

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Bacteriology —Gram positive cocci can be seen in large numbers in smears made of the stool The stool should be cultured on blood agar for diagnosis, and a heavy growth of staphylococci will

any broad spectrum drug or combination of drugs with suppressive activity against coliforms should be discontinued immediately

Some investigators have suggested the use of staphylococcal antitoxin however the antigenicity of enterotoxin is variable and commercial antitoxins are standardized against alpha toxin and not enterotoxin

Patients with postantibiotic staphylococcal enteritis present a very difficult problem in fluid balance A liter an hour for half a day or longer may be required to keep them hydrated A detailed intake and output chart is of course essential and the patient should be nursed in strict isolation

PROGNOSIS —The prognosis of staphylococcal enteritis will be directly related to the time elapsing between onset and the institution of adequate treatment In one series of 23 cases 19 of them were fatal Other series have shown a lesser mortality rate

STAPHYLOCOCCAL GASTROENTERITIS IN THE NEWBORN

PATHOLOGY —Newborn infants with this disease show many of the same effects which are found in adults The main findings at autopsy are in the gastrointestinal tract and are similar to those described in the preceding section

BACTERIOLOGY —Gram positive staphylococci are present in large numbers in the stool We find that *Staphylococcus aureus* will grow on culture on nonselective media Blood cultures are usually sterile

INCIDENCE —Staphylococcal gastroenteritis has a way of occurring in epidemics affecting as many as 60% of the children in a nursery

CLINICAL PICTURE —If this disease attacks during the first week of life there is an abrupt onset of severe retching and vomiting followed by diarrhea The infant is listless bowel sounds are diminished or absent the stools are watery green and frequent It may be noticed that other babies in the nursery have a milder

from the upper intestine may increase enormously in volume and have a rice water appearance

In occasional cases shock will precede diarrhea and cause diag nostic difficulty The blood pressure should be taken frequently throughout the course of the illness to detect the onset of shock

LABORATORY DIAGNOSIS —The white cell count rises usually to *15–25 000/cu mm, but it has been recorded as high as 60,000/* cu mm A moderate rise in blood urea nitrogen and a fall in serum albumin can be noted

PREVENTION —To prevent this complication certain things should be avoided One of them is purgatives which may precipi tate the condition Another is antibiotics, which should be used only when definitely indicated and if possible a narrow spectrum antibiotic should be employed Doses of tetracycline over 1 Gm per day lead to enteritis more often therefore 1 Gm dosage is preferred, but it is important to emphasize that this dosage is not adequate for certain serious infections

TREATMENT —This disease constitutes an emergency, and a bare suspicion of its presence is adequate reason for starting treat ment Before deciding which of several effective drugs should be used, it would be well to remember that the organism which causes postantibiotic staphylococcal enteritis has almost always been acquired in the hospital Therefore it will probably be very highly resistant to the most commonly used antibiotics Another important fact to be considered is that there is an enormous amount of fluid present in the upper gastrointestinal tract This means that oral medication alone cannot be relied on especially in severe cases For initial use novobiocin is favored over other drugs both for oral and parenteral use Bacitracin and neomycin are suitable for oral use and staphylococci are not usually resist ant to them Erythromycin is no longer considered useful because overuse has destroyed its effectiveness It is important not to use any antibiotic with killing effect on gram negative organisms un less in vitro sensitivities definitely point to its usefulness Medica tions which the patient has been getting must be checked and

phragm may suggest intra abdominal disease There may occur an extension of infection to the muscles of the loin, downward to point at the groin medially to rupture into the abdomen upward to form a subphrenic abscess or perforate the diaphragm or very infrequently, into the colon

LABORATORY DIAGNOSIS —The urine is usually normal but occasionally some protein and pus cells are present *Staphylococcus aureus* may grow on culture Chest x rays should be taken since it was found that in one series 10% of cases had perinephrobronchial fistula Tests show that leukocytosis is always present and there is frequently anemia A negative aspiration of a suspected abscess may be misleading so an exploration should be done if the diagnosis is likely

RADIOLOGY —The only specific indication of this disease on x ray is extravasation of the contrast material into the perirenal area We may find that the psoas shadow is absent The normal excursion of the kidney (not less than one vertebra) is decreased On lateral pyelogram the kidney is displaced forwards Occasionally osteomyelitis of the ribs or vertebrae is present In about one fifth of the cases there is an associated calculus

TREATMENT —In early cases of perinephric abscess it is possible that intensive appropriate antibiotic therapy will be curative However patients are never too ill for exploration and if there is fluctuant pus present surgery is indicated A drain should be inserted and the wound left open In certain cases a renal lesion or a calculus may need to be dealt with at a later operation Any renal infection should be dealt with as noted under renal carbuncle

PROGNOSIS —Figures for mortality with combined antibiotic and surgical treatment are not available Before we had antibiotics children who had renal disease in addition to perinephric abscess (characterized by many pus cells in the urine) had a mortality rate of 45% Without intra renal disease there was no mortality

diarrheal illness Very ill children may develop intermittent toxic contractions of all muscles or severe necrotic skin lesions.

RADIOLOGY —An absence of the normal intestinal gas pattern is noted on x ray

PREVENTION —Epidemics are to be deplored because the care ful control of cross infection in newborn nurseries will prevent this disease

TREATMENT —For very mild cases a satisfactory program may be water by mouth for 8 hours followed by an oral amigen elec trolyte mixture and then formula devoid of sugar However the maintenance of an adequate fluid balance is very important espe cially in the severe cases Quite often parenteral Ringer s solution is recommended Appropriate oral antibiotic treatment usually suffices to relieve symptoms Incidentally the tetany like symp toms do not respond well to intravenous calcium

PROGNOSIS —Deaths from staphylococcal gastroenteritis are rare Mild diarrhea will usually run its course in a few days Even the serious disease lasts less than a week

PERINEPHRIC ABSCESS

BACTERIOLOGY —This disease is most frequently caused by *Staphylococcus aureus*

INCIDENCE —Adults are the most often affected by perinephric abscess but it has also been observed in the very young

CLINICAL PICTURE —The general symptoms of perinephric abscess are malaise weight loss chills and sweating There is usually a constant dull ache in the costovertebral angle made worse by pressure in the lumbar region The pain may be in creased by *hyperextension of the hip joint and there is some in* ability to bend toward the uninvolved side Such symptoms as distention vomiting cough, dyspnea or diarrhea may be present Urinary symptoms are rare Examination may reveal a warm red edematous mass in the loin The breath sounds are dimin ished *A rigid abdomen* which is a result of fixation of the dia

with and following surgery Treatment for at least 2 weeks is indicated and a month or longer may be necessary

PROGNOSIS —If a follow up check is made 6 months to a year later it usually shows a kidney which is functionally and anatomically normal

SUBPHRENIC ABSCESS

PATHOLOGY —These abscesses are most often found in the right suprahepatic area the right side being three times as common as the left About 10% of cases have a serous pleural effusion and about 20% have empyema

BACTERIOLOGY —The most frequent causes of subphrenic abscess are streptococci coliforms and staphylococci In about 7% of cases cultures are sterile the remainder are equally divided between pure and mixed cultures *Staphylococcus aureus* is an uncommon single cause of this condition—it is responsible for only 10–20% of cases

INCIDENCE —Males predominate 2 1

PREDISPOSING FACTORS —Subphrenic abscess frequently follows a perforated peptic ulcer (30%) appendicitis (20%) or abdominal operations (15%) Less often we find it complicating penetrating wounds biliary disease or carcinoma of the alimentary tract

CLINICAL FEATURES —The patient generally complains of tenderness and swelling on the side of the abscess and also of pain in the right upper quadrant Other common symptoms are vomiting and distention cough with sputum and dyspnea and diarrhea which may be of serious import This is accompanied by a continuous swinging fever of 100–102 F There may be a dull percussion note at the base of the lung with poor air entry Clubbing indicates an intrathoracic complication

RADIOLOGY —Absence of radiological change does not exclude this disease A raised thick poorly defined diaphragm suggests the presence of an abscess In 15–30% of cases gas is present in

RENAL CARBUNCLE OR ABSCESS

PATHOLOGY —A renal carbuncle forms where a series of small abscesses have combined to form one large abscess We may find sloughs of kidney tissue present If the abscess is long standing it may have burst into the perinephritic tissues or renal pelvis Most often only one kidney is affected

BACTERIOLOGY —Renal carbuncle is caused without exception by *Staphylococcus aureus*

INCIDENCE —This is a very rare disease

CLINICAL FEATURES —The patient first complains of moderate fever anorexia and aching pain in the loin There may be a history of sepsis of the skin in the preceding months Upon examination one finds tenderness in one loin associated with a smooth tender swelling of the tissues The mass felt on bimanual examination is usually fixed but occasionally it will move slightly on respiration A noticeable reduction in symptoms and signs usually means that there has been rupture into the renal pelvis—this is indicated by gross pus in the urine

LABORATORY DIAGNOSIS —Leukocytosis is regularly found Staphylococci may be grown on culture from the pus obtained at operation Usually the blood urea nitrogen and creatinine are normal or only slightly elevated Pyuria is uncommon and the urine may be normal in all respects on routine examination

RADIOLOGY —Poor function of one kidney is a usual but not invariable finding The outline of an enlarged kidney may be seen The calyx nearest to the mass may be deformed

TREATMENT —Surgery for renal carbuncle is urgent as delay in treatment may cause increased damage to the kidney tissue The kidney should be exposed and the contents of the abscess scraped out with the finger or as as alternative the area could be excised with diathermy One to two hundred cc of pus may be obtained in this process Nephrectomy should rarely be necessary It is wise to use a prolonged antibiotic treatment starting

in the 30–50 age group There is no difference in incidence in different racial groups

PREDISPOSING FACTORS —Liver abscess most frequently follows appendicitis although at times there is no obvious preceding infection Other cases follow such diseases as cholecystitis other types of gastrointestinal sepsis or abdominal trauma

CLINICAL FEATURES —The onset of a liver abscess is acute with fever chills and marked sweating A dull constant pain and tenderness are complained of in the right upper quadrant although sometimes patients have this pain in the right lower chest If the disease remains undiagnosed for some time, anorexia malaise and weight loss become noticeable Jaundice and ascites are uncommon being seen in less than a quarter of the patients Nausea and vomiting are rare and should suggest the presence of some other disease On examination the liver is usually enlarged and the tenderness is confirmed

RADIOLOGY —This is frequently very helpful You will find that elevation and immobility of the diaphragm are seen most often on the right side If an examination of the barium filled upper gastrointestinal tract is made it may show that an abscess of the left lobe has deformed the lesser curvature of the stomach Angiography may also help

LABORATORY DIAGNOSIS —A leukocytosis of 15–25 000/cu mm is found with a predominance of young cells Albuminuria is occasionally present Exploration with a needle should not be done

PREVENTION —The best prevention is the careful early diagnosis and treatment of appendicitis and other intra abdominal *sepsis which used to lead to many cases of liver abscess*

TREATMENT —When the abscess is single surgery is the main treatment and for this an extraperitoneal anterior or posterior approach to the liver is the most satisfactory Antibiotic coverage with chloramphenicol at the time of operation can be followed by more definitive therapy when a bacteriological diagnosis has been made If multiple abscesses appear to be present intensive prolonged chemotherapy is necessary Because the causative or

the abscess When fluoroscoped, the diaphragm will be seen to be fixed

TREATMENT —Surgery is a necessity here before operating, it is only necessary to know on which side the abscess is situated Exploration is preferred to aspiration Surgical drainage should be aided first by therapy with a streptomycin tetracycline combination (in expectation of a coliform organism) and later with the drug indicated by in vitro testing of the pus obtained at operation

PROGNOSIS —There is an overall mortality of 40% Age has an unfavorable effect Cases occurring *de novo* have the best prognosis, whereas those following biliary disease or carcinoma have the worst Multiple space abscesses are worse than those in a single space and those on the left are worse than those on the right Those patients who have serious complications do poorly, emphasizing the need for early diagnosis Extra serous drainage combined with appropriate chemotherapy improve the prognosis

LIVER ABSCESS

PATHOLOGY —The most obvious feature of this abscess is the enlargement of the liver to twice its normal size The right lobe of the liver since it receives the portal blood draining the superior mesenteric region, is the most often involved One may be surprised to find a primary focus of sepsis in the appendix or gall bladder, and occasionally a generalized pyemia is present Two-thirds of the cases seen have multiple abscesses varying in size ½–1 centimeter in diameter Sometimes rupture has occurred into the peritoneum or the chest or under the diaphragm

BACTERIOLOGY —*E coli* is the predominant cause (30%) with streptococci (20%) staphylococci (17%) and a mixture of these organisms (17%) being other causes Occasionally the pus is sterile

INCIDENCE —This is a rare disease which constitutes only 01–0 5% of autopsies *Fewer cases occur after appendicitis nowadays* so the age incidence is higher than it was most of the cases falling

6 / SEPTICEMIA AND ENDOCARDITIS

SEPTICEMIA OCCURS when natural host resistance is over whelmed but the disease continues only because of continual seeding of the blood stream from some primary focus Many pa tients die with this disease undiagnosed because no one was alert to this possibility Unfortunately others die even after intensive well directed therapy There is a great need for improvement in both diagnosis and therapy

The three diseases described in this chapter have features in common yet they are different enough to merit the separate dis cussions that follow

STAPHYLOCOCCUS AUREUS SEPTICEMIA

DEFINITION —Septicemia is the clinical condition in which bacteria in the blood stream cause systemic symptoms and signs such as high fever chills and malaise

PATHOLOGY —Lesions are found most frequently in the respir atory and in the genitourinary organs In a minority of cases local skin abscesses produce or constitute the initial infection

Examination of the lung often reveals lobar or lobular pneu monia which is usually hemorrhagic Squeezing an area of con solidated lung yields a mixture of yellow pus and blood Areas of necrosis occur In about a quarter of the cases pulmonary ab-scesses or septic emboli are found Empyema is surprisingly rare in adults though it is less rare in children

ganism is initially unknown, combined treatment with penicillin sulfonamide and chloramphenicol is recommended This treatment should be continued for 6 weeks or for 2 weeks after the patient is afebrile whichever is the longer

PROGNOSIS —The mortality from liver abscess without antibiotics has ranged from 50–90% Cases following appendicitis are grave, because multiple abscesses are frequently present Complications, particularly pleural or pulmonary ones worsen the outlook and the presence of jaundice indicates a serious prognosis If the patient has a concurrent pyemia, the disease is commonly fatal

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per cc. of blood This still has a prognostic value Occasionally the antibiotic sensitivities of the organism isolated from the blood may change When this occurs a super infection has taken place as the phage type is different

INCIDENCE —This is an infection of the extremes of life All ages may suffer but it is most common in those under 10 or over 50

The sex incidence is maintained throughout most of the age periods in the ratio of 2 males to every female The exceptions to this statement are a relatively larger number of females in the 0–9 age group and in the 40–49 age group In groups over 70 years there are 5 males to every female This may be explained partly by the number of cases occurring after transurethral resec tion of the prostate No particular difference has been shown for different nationalities or amongst the Negroid and Caucasian races

This disease occurs at the rate of 2–9 cases per thousand ad missions in large general hospitals A study of autopsy statistics show that the cases of death from primary staphylococcal septi cemia make up 5% of total autopsies Several observers have found that the incidence is remaining steady whereas I agree with those who find that within the past few years there has been a rise in the number of cases occurring in hospital at least to the level which was prevalent before the use of antibiotics

PREDISPOSING AND PRECEDING FACTORS —In the past the most important preceding cause of septicemia has been transurethral resection of the prostate In different series 10–25% of the total is made up of such cases In the past 5 years however about 25% of the cases in large series are persons receiving cortisone or ACTH About 10–20% have neoplastic diseases most often leu kemia or lymphoma Approximately 10% are diabetics often first discovered at the time of septicemia Many patients who have exfoliative dermatitis die of staphylococcal septicemia The isola tion of the staphylococcus from the blood is of grave prognostic significance About 40–50% of the patients with this disease have

Usually multiple abscesses are found throughout the genitourinary tract and in a few cases chronic pyelonephritis is present Abscesses in the prostatic perirenal uterine or bladder areas may occur but are rare Infrequently cases of true pyemia are seen with abscesses in the lung kidney brain, myocardium and subcutaneous tissues Petechiae are rare in the absence of endocarditis Involvement of the liver is uncommon and jaundice is unusual, at least in adults

The cardiovascular system is involved in only 5–10% Endocarditis may occur The large friable vegetations occur most often on the mitral valve less often on the mitral and aortic Rarely the tricuspid or pulmonary valves are damaged as in drug addicts who have given themselves intravenous injections without aseptic precaution If the myocardium is involved we find that the usual lesions are discrete abscesses but rarely a diffuse myocarditis is present Pericarditis is fairly common as the predominant cardio *vascular lesion*

The bone lesions of a preceding osteomyelitis may be found at autopsy but septicemia is not a common *late* complication of osteomyelitis Adrenal gland abscess or necrosis is observed in only about 3% of cases but is a serious complication Abscess of the spleen is occasionally found

Bacteriology —The organism is a coagulase positive hemolytic *Staphylococcus aureus* In a small number, probably not exceeding 1% *Staphylococcus albus* has been recovered repeatedly It may or may not be hemolytic or coagulase positive Isolation of both organisms is extremely rare although it does occur after partial mutation of aureus strains to albus In my experience three blood cultures are adequate to diagnose the great majority of staphylococcal septicemias Cultures taken during life rarely show a mixed infection but *Staphylococcus albus Streptococcus viridans* or *E coli* have on occasion been isolated along with *Staphylococcus aureus* If the patient has received antibiotics bone marrow cultures may still be positive when venous blood is sterile It used to be the custom to count the number of colonies

per cc of blood This still has a prognostic value Occasionally the antibiotic sensitivities of the organism isolated from the blood may change When this occurs a super infection has taken place, as the phage type is different

INCIDENCE —This is an infection of the extremes of life All ages may suffer but it is most common in those under 10 or over 50

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some predisposing cause About 25% of children have predispos ing factors compared with 85% of adults

CLINICAL FINDINGS —Fulminating, rapidly fatal staphylococ cal septicemia is rare contrary to prevalent opinion Not more than 1% of cases have such a course The onset is usually moder ately rapid but not fulminating The patient generally feels cold and ill and may be confused There are no characteristic symp

TABLE 3 —ANTIBIOTIC DRUGS OF CHOICE IN THE TREATMENT OF STAPHYLOCOCCAL DISEASE

ORDER OF PREFERENCE	DRUGS	COMMENTS
1	Penicillin	Outstanding
2	Streptomycin	Many resistant strains
2	Erythromycin	Low toxity
2	Novobiocin	May produce a rash
3	Chloromycetin*	For life threatening infections
3	Ristocetin	Has to be given intravenously
3	Vancomycin	Has to be given intravenously
3	Kanamycin	Has to be given intramuscularly
4	Furadantin	When given intravenously or orally for urinary tract infections
4	Tetracycline*	Many resistant strains
4	Bacitracin	Mainly for oral or local application
4	Neomycin	Local application
	Sulfa	Only as additional drug or for special problems with resistant strains
	Oleandomycin	

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toms or signs Anorexia nausea vomiting hiccup abdominal pain and diarrhea are fairly common In a few arthralgia or myalgia occur The temperature is usually 103° F or higher

The initial diagnosis is frequently not septicemia but pneu monia, heart failure pyelonephritis or fever of unknown origin Even alert clinicians can make the correct diagnosis in only about one third of cases

Albuminuria occurs in about 75% of patients and about half of these have hematuria Leukocytosis with more than 10 000 cells per cu mm occurs in about 65% of cases About 30–50%

of cases have anemia Increased sedimentation rate is usual

TREATMENT —Initially penicillin or if contraindicated erythromycin should be given if the disease was acquired outside the hospital chloramphenicol and novobiocin if the disease was acquired inside After sensitivity tests the drugs listed in Table 3 can be chosen according to in vitro sensitivity Early adequate treatment is of prime importance and treatment should be continued for 6 weeks Sometimes when blood cultures become sterile following treatment a single blood culture may disclose staphylococci If the organism is susceptible to the antibiotics being used this need cause no alarm but it does indicate the need for prolonged treatment Failure of the temperature to fall within the first week of treatment should lead to a search for abscesses The skin renal and perirenal tissues and the pelvis should be searched by all available technics Empyema should be excluded also When the temperature is normal or nearly so the patient should be encouraged to move around to avoid thrombophlebitis and subsequent pulmonary embolism

PROGNOSIS —When patients are treated with the antibiotics indicated by in vitro sensitivity tests the temperature usually becomes normal within 5–7 days Sixty four per cent of fatalities occur within the first month and 82% within the first 2 months Seventy per cent of surviving patients have a hospital stay of 2 months or less With successful treatment the disease seldom lasts more than 3 months

There are no major residuae following staphylococcal septicemia in surviving patients Infections of the respiratory system and the kidneys are of major importance in prognosis Chest x rays pyelograms repeated tests for BUN's and creatinine may help in judging a prognosis In untreated cases a temperature of under 102 F and a white cell count below 10 000 per cu mm are associated with poor prognosis With treatment however there are some survivors in this group The best prognosis is in patients with a maximal temperature between 102–104 C and with a maximal white cell count between 10 000 and 20 000

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is present. Frequently there is pain in the shoulder and in the knee and ankle joints but generalized joint aches are not uncommon Rashes usually of a morbilliform type, are common The most frequent finding on examination is a cardiac murmur generally systolic in nature and heard best at the apex Rarely a pericardial friction rub may be heard The spleen is only palpable in about one quarter of the patients Central nervous system involvement is common being shown in many ways such as delirium confusion stiff neck or hemiplegia Leukocytosis is present As the disease progresses a mild anemia develops with the hemoglobin usually about 9 Gm per 100 cc

DIAGNOSIS —Diagnosis is made by the isolation of *Staphylococcus albus* in two or more cultures from the blood Sometimes the organism may also be cultured in the urine

RADIOLOGY —Occasionally infiltrations in the lungs are found. In some cases osteolytic lesions have been seen

DIFFERENTIAL DIAGNOSIS —The clinical picture of this disease is much more suggestive of subacute bacterial endocarditis due to *Streptococcus viridans* than to a *Staphylococcus aureus* septicemia Other causes of a mild prolonged fever have to be eliminated

TREATMENT —This is identical to that given for *Staphylococcus aureus* septicemia

PROGNOSIS —Mortality of the untreated disease is approximately 70–75% The response to treatment is about the same as in the aureus disease

STAPHYLOCOCCAL ENDOCARDITIS

DEFINITION —There is no difficulty in recognizing endocarditis at autopsy It has been suggested that this diagnosis can be made during life in those who have repeatedly positive blood cultures in the presence of definite signs of some type of valvular disease which may or may not have been present at the onset of the infection Significant changes in the character of the murmurs

Anemia with less than 10 Gm of hemoglobin or less than 3 million red cells per cu mm is present in about one third of cases It does not seem to have any bearing on prognosis Infections acquired in a hospital generally have a poorer outlook, since the strains frequently are resistant to a number of antibiotics and treatment is thus more difficult The portal of entry affects the prognosis as entry through the respiratory tract through surgical wounds or following a transurethral resection operation is associated with a high mortality rate while septicemias following bone and joint infections or those with an unknown portal of entry are associated with a lower mortality

STAPHYLOCOCCUS ALBUS SEPTICEMIA

DEFINITION —*Staphylococcus albus* septicemia is present when *Staphylococcus albus* is isolated on two or more occasions from the blood of a person who has a septicemia and from whom no other pathogens are isolated by blood culture

BACTERIOLOGY —*Staphylococcus albus* is a staphylococcus which produces porcelain white or indifferently colored colonies but never produces a yellow or golden pigment Usually these organisms are coagulase negative and do not ferment mannitol

INCIDENCE —All age groups can be affected but this occurs most often in neonatal children and in puerperal women A 2 1 preponderance of males is observed in this disease as in *Staphylococcus aureus* septicemia

PREDISPOSING FEATURES —This is predominantly a disease of patients with reduced host resistance Many of them have had rheumatic fever in the past and a number develop the disease following operation or transfusion

CLINICAL FEATURES —The onset is insidious with a gradual malaise and fever frequently followed by shaking chills The patients complain mainly of symptoms referable to the cardiovascular or respiratory systems or the bones and joints Dyspnea cough and sore throat are common and occasionally pleuritic type pain

is present. Frequently there is pain in the shoulder and in the knee and ankle joints, but generalized joint aches are not uncommon Rashes usually of a morbilliform type are common The most frequent finding on examination is a cardiac murmur generally systolic in nature and heard best at the apex Rarely a pericardial friction rub may be heard The spleen is only palpable in about one-quarter of the patients Central nervous system involvement is common being shown in many ways such as delirium confusion stiff neck or hemiplegia Leukocytosis is present As the disease progresses a mild anemia develops with the hemoglobin usually about 9 Gm per 100 cc

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while under observation, or embolic phenomena of more than transient nature involving the skin brain, lungs, kidneys or other peripheral arteries or petechiae, are taken as further evidence in favor of endocarditis

PATHOLOGY —The valves are affected in the following descending order of frequency mitral mitral and aortic, tricuspid and pulmonary

BACTERIOLOGY —*Staphylococcus aureus* is isolated 4–5 times as frequently as *Staphylococcus albus* In a very occasional case there may be a mixed infection with staphylococcus and a streptococcus or other organism

INCIDENCE —In Thayer s large series of 536 endocarditis cases *Staphylococcus aureus* was responsible for 6 9% and *Staphylococcus albus* for 1 3% At the time of this report in the 1930 s, the ratio of streptococcal to staphylococcal endocarditis was 7 4 1 whereas in the 1940 s the ratio was 2 6 1 A small part of this increase is due to addicts who inject narcotics directly into the blood stream It has been calculated that there were approximately 280 cases per year of staphylococcal endocarditis in the United States Approximately equal numbers of males and females are affected and the ages of the majority of these patients fall within the third and fourth decades

PREDISPOSING FACTORS —About 50% of these patients have preceding chronic rheumatic valvular disease and 25% have arteriosclerotic or syphilitic heart disease or chronic cor pulmonale The remainder have normal hearts In a recent survey endocarditis was found in every instance of staphylococcal septicemia with significant valvular disease Narcotic addicts develop this disease frequently Staphylococcal endocarditis has been described following mitral valvulotomy These cases have been due both to aureus and to albus strains

CLINICAL FEATURES —Initially the onset is that of an acute infectious disease with marked chills Other complaints are of fever sweats anorexia and loss of weight or malaise In some cases embolization occurs, and in others congestive cardiac failure is

found Petechial eruptions are very common and are almost but not completely, diagnostic of endocarditis in the presence of a positive blood culture A rapid course is not uncommon In some patients the signs and symptoms of onset may suggest encephalitis

LABORATORY TESTS —The diagnosis depends on isolating etio logic agents from the blood on two or more occasions in patients with cardiac murmurs

DIFFERENTIAL DIAGNOSIS —This is difficult but clubbed fingers and a palpable spleen would suggest streptococcal endocarditis Arthritis cough chest pain meningismus or subcutaneous ab scesses would suggest staphylococcal endocarditis

TREATMENT —The treatment is the same as that for staphylo coccus septicemia Massive doses of penicillin are the main factor in recovery from this disease A period of 4–6 weeks of treatment is recommended

PROGNOSIS —The fatality rate does not differ in those infected with an aureus or an albus strain The age of the patient is im portant Those over 50 have a poorer outlook A delay between onset and treatment affects prognosis adversely

FURTHER READING

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Smith I M Vickers A B and Willis P The natural history of 338 treated and untreated cas s of staphylococcal septicemia (1936 1955) Submitted to Lancet 1958

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7 / MISCELLANEOUS PROBLEMS

MENINGITIS

THE DIAGNOSIS of meningitis was first confirmed bacterio logically by Galippe in 1889 Drainage of the cerebrospinal fluid intravenous *gentian violet bacteriophage and various* other treatments were subsequently tried, but the development of the sulfonamide drugs provided the first effective therapy

PATHOLOGY —In staphylococcal infection, the meninges are most frequently infected via the blood stream but direct spread from without may follow fracture cranial osteitis (especially mas toiditis), infection of the nasal sinuses or of the soft tissues of the scalp lumbar puncture or craniotomy

We must remember that the cerebrospinal fluid space is virtu ally defenseless because of low antibody titer and lack of fixed tissue defense cells

Large amounts of purulent discharge tend to collect over the very vascular convex surfaces of the cerebrum Multiple abscesses are found in the cortex but they are usually not more than 1 cm in diameter Blockage of the flow of cerebrospinal fluid is not a marked feature but it may result from inflammatory adhesions in the cisternal magna obstructing the outflow of cerebrospinal fluid from the fourth ventricle

INCIDENCE —Staphylococcal meningitis is rare In a total of 1,535 cases of meningitis only 11 cases were due to this organism In one series 38% of those with staphylococcal septicemia de

veloped meningitis it was observed in 54% of those with septi cemia plus endocarditis but in only 10% of those with septicemia alone.

CLINICAL PICTURE —The signs and symptoms of meningitis are not different from those of any other purulent meningitis they tend to vary with different age groups

In infants fever vomiting drowsiness convulsions and bulging of the fontanelle are present Newborns may be cyanotic Older children complain of headache they are febrile drowsy vomit and may convulse A stiff neck is present on examination In adults stiff neck and headache are the main findings Other evi dence of staphylococcal disease may be present and as a number of these cases are secondary to endocarditis examination of the heart may reveal this diagnosis

A relatively localized spinal form of the disease sometimes oc curs It may follow osteomyelitis of the vertebrae or it may follow an abscess which develops close to the vertebrae Rarely it is introduced by lumbar puncture or operation The onset is usually gradual with severe low back and thigh pain The legs are held in flexion and leg straightening causes severe pain Constipation is commonly accompanied by urinary retention The lower limb re flexes are absent but sensory changes are inconstant Frequently upward extension of the infection rapidly changes the clinical picture to that of generalized cerebrospinal meningitis

LABORATORY DIAGNOSIS —A definitive diagnosis can only be made after lumbar puncture In the absence of papilledema lum bar puncture should be a fixed diagnostic procedure for febrile convulsions Examination of the cerebrospinal fluid shows the following

Pressure increased

Naked eye appearances turbid to purulent possibly xanthochromic Sometimes a fine coagulum forms

Cells up to thousands per cc predominantly polymorphs Large mononuclear cells are frequently seen A leakage of red cells into the spinal fluid is common

Protein increased In purulent fluid it may attain 500 mg per cent

Chlorides these reflect the serum level but are usually 650-680 mg per cent
Glucose recedes rapidly from the usual level of 60–80 mg per cent. A good practice is to do a 6 tube test for sugar *
Lange s colloidal gold meningitic type viz. 0012344310
Smear best made with methylene blue or Wright s stain but a second smear stained with Gram s method is useful Staphylococci are usually very numerous
Culture on both solid and liquid media

TREATMENT —Several aspects of treatment will be discussed under this heading

1 *Nonspecific treatment* Patients with meningitis benefit from complete rest Intramuscular paraldehyde 0 2 cc of a 5% solu tion per kilogram is recommended if there is great restlessness Convulsions can best be controlled by the use of chloroform Dehydration is very common and the best way of replacing fluids is through a stomach tube In cases of the localized spinal form of meningitis surgical drainage by laminectomy is recommended In an occasional case local intracranial collections of pus may be drained

2 *Treatment while awaiting diagnosis* If a diagnosis cannot be made on a direct smear of the cerebrospinal fluid the patient will have to be treated as a case of meningitis due to unknown bacteria In this case the best treatment is a combination of sulfa diazine penicillin and chloramphenicol

3 *Specific treatment*

SULFONAMIDES Although a few cases have recovered with this treatment these drugs are no longer recommended Application of sulfonamides to the brain directly is irritant and causes con vulsions

PENICILLIN Even large parenteral doses such as 10–25 million units per 24 hours give a level of only between 03 to 21 units per cc (1 unit effective) in the cerebrospinal fluid Many pa tients however have recovered after *large* parenteral doses of

*See Alexander H E in Levine S Z (ed) *Advances in Pediatrics* (Chicago Year Book Publishers Inc 1947) vol II

penicillin probably due to the greater permeability of the blood brain barrier when it is inflamed Intravenous penicillin may therefore be tried in treatment but a poor clinical response should lead one to change to more effective treatment as noted below Penicillin applied directly to the brain is irritant and should not be used in doses greater than 10 000 units intrathecally

BACITRACIN This antibiotic has been used successfully to treat certain cases of staphylococcal meningitis For treatment 5 000 10 000 units are dissolved in 3–5 cc of normal saline solution and given intrathecally once or twice a day for 5–10 days In addition 25 000 units can be given every four hours intramuscularly for the same period Unfortunately we find that certain strains are not susceptible to this antibiotic and its use must therefore be preceded by some knowledge of the sensitivity of the organisms A favorable consideration is that there are no tissue antagonists to this medication

CHLORAMPHENICOL This is a drug which penetrates into the subarachnoid space in adequate quantities and is the drug of our choice It should be given in high dosage Should the patient fail to respond to this parenteral penicillin and sulfa may be tried while in serious cases intrathecal bacitracin should be used

4 *The treatment of shock* Shock does not usually occur after the first day but in the initial hours of treatment the patient must be observed closely for it Cold and clammy extremities are a warning sign The blood pressure should be recorded every half hour The treatment of shock is by norepinephrine 4 cc to 16 cc of 1 in 100 000 solution in 500 cc of intravenous fluid The giving of this solution must be controlled by careful and frequent estimation of the blood pressure

PROGNOSIS —The alertness of the patient at the beginning of treatment is the single most important prognostic sign The sooner treatment is started the better will be the prognosis If the intracranial pressure exceeds 400–500 mm cerebral anoxia is inevitable If the proportion of bacteria to leukocytes in the spinal fluid is large it is believed that one must expect a poor prognosis The

prognosis also depends somewhat on the form of the disease for the localized spinal form has a much better outlook than the generalized form When the patient begins to improve, the white cell count of the cerebrospinal fluid will rise, and this sign will be a welcome one and should not be erroneously regarded as it sometimes is, as a bad sign Recurrences of meningitis are rare

AGAMMAGLOBULINEMIA

This is an absence of serum gamma globulin Usually a deficiency of immunoglobulin leads to an increased susceptibility to infection Pulmonary infections and meningitis are the most common infections found but many complications, usually bacterial in origin can occur At least 20% of cases described so far have had staphylococcal infections In *congenital agammaglobulinemia* increased susceptibility to infection in infancy or childhood is confined to males partly on a genetic background This is a permanent defect. *Acquired agammaglobulinemia* occurs in infants of either sex and is of limited duration It is thought that there is a delay in the onset of normal gamma globulin synthesis in the first 6 months of life after the decay of the gamma globulin received from the mother The defect can be *acquired in adults* in relation to a disease of the reticulo endothelial system such as malignant lymphoma or lymphatic leukemia It may also be idiopathic or may be associated with a general hypoproteinemia as for example in nephrosis Some cases are associated with enlargement of the spleen

TONSILLITIS

PATHOLOGY —The red enlarged tonsil has pus filling its crypts and microscopic examination shows loss of the epithelium of the crypts which are increased in size and filled with purulent exudate and fibrin The tonsillar substance may be infiltrated with polymorphs and an abscess may form Chronic inflammation results

in fibrous tissue cholesterol and calcium scattered throughout the tonsil.

BACTERIOLOGY —The great majority of cases of suppurative follicular tonsillitis is caused by Group A hemolytic streptococci, but a small and possibly an increasing fraction is caused by hemolytic *Staphylococcus aureus* Another small group is caused by Group B *H influenzae*

INCIDENCE —Staphylococcal tonsillitis is rare

PREDISPOSING FACTORS —Patients hospitalized for other reasons particularly after manipulations in the oral cavity or following the use of indwelling oral or nasal tubes may develop staphylococcal tonsillitis The use of broad spectrum antibiotics also predisposes to this infection

CLINICAL FEATURES —The onset is abrupt with a high fever (102–106° F) dysphagia chills and malaise Headache nausea and vomiting are frequent A follicular tonsillitis is frequently accompanied by an exudate on the soft palate and edema of the whole of the tonsillar beds and soft palate The tonsillar lymph nodes at the angle of the jaw are swollen and acutely tender and in a few cases a membrane may form There is no clinical method of differentiating this from the much more prevalent streptococcal tonsillitis One should be alert to the possibility of staphylococcal tonsillitis in the patient with tonsillitis who fails to respond to penicillin within 24 hours particularly if the disease has been acquired in hospital

LABORATORY DIAGNOSIS —Staphylococci cannot readily be differentiated from streptococci in a smear and the diagnosis of tonsillitis depends on culture The leukocytosis usually exceeds 20 000 per cu mm The differential white cell count helps to rule out infectious mononucleosis The results of throat culture will exclude diphtheritic and monilial infection

TREATMENT —These patients should be isolated with mask and gown isolation until the purulent character of the tonsillitis has disappeared or until negative cultures are obtained A liquid

diet is comforting The best antipyretic and analgesic is prompt *specific treatment but aspirin and codeine may be helpful ini*tially in some patients Initial systemic treatment with erythromycin or novobiocin in 2 Gm doses daily by mouth in divided doses, is recommended This can be changed later if necessary after in vitro tests

OTITIS EXTERNA

PATHOLOGY —The lining of the external auditory canal is edematous and superficial epithelial cells, pus fibrin and organisms fill the lumen

BACTERIOLOGY —*Pseudomonas aeruginosa* is the predominant causal organism (26%) with *Staphylococcus albus* (22%), *Staphylococcus aureus* (15%) *E coli* (8%) and *Proteus* (6%) being the next most frequent causes

INCIDENCE —This common disease affects both children and adults

PREDISPOSING FACTORS —Moisture especially from swimming and warm weather are common precipitating causes Trauma from fingernails bobby pins and similar objects initiate or aggravate the disease

CLINICAL FEATURES —Early itching or pain in the external auditory canal is followed by a purulent discharge The patient will notice that the pain is made worse by eating or by touching the ear as it also is by handling the pinna and the use of the otoscope The drum is usually normal but the pre and post auricular glands—and sometimes the cervical glands—are enlarged and tender The meatal wall is edematous and a grayish mixture of waxy purulent material and desquamated cells is present in the canal

LABORATORY DIAGNOSIS —It is necessary to identify the etiological agent by culture and establish its antibiotic sensitivities

DIFFERENTIAL DIAGNOSIS —Otitis externa has to be distinguished from chronic suppurative otitis media and a co-existing otitis media has to be excluded

TREATMENT —The most important procedure is to clean the canal of wax and debris Freedom from water is of paramount importance Packing with sterile gauze soaked in aluminum acetate solution is beneficial in the acute stages Later an alcoholic solution of gentian violet should be used

An acid reaction is inhibitory to most of the causative organisms so that household vinegar dropped into the ear 6-8 times daily is a useful domestic remedy If an antibiotic is to be used a polymyxin ointment or a polymyxin neomycin combination is indicated Drops of the same type may penetrate better

PROGNOSIS —Relapses are common

ACUTE OTITIS MEDIA

PATHOLOGY —Edema of the eustachian tube and the mucosa of the middle ear are followed by accumulation of serous mucoserous or purulent fluid If untreated the exudate may lead to fibrous adhesions

BACTERIOLOGY —Approximately 40% of cases of otitis media are caused by pneumococci 25% by *Staphylococcus aureus* 3% by *Streptococcus viridans* and 16% by *H influenzae* The remaining 16% are sterile on culture The preponderance of Gram positive cocci or upper respiratory tract pathogens where the infection enters via the eustachian tube contrasts with the prevalence of Gram negative rods or bowel pathogens in chronic suppurative otitis where the infection enters via the external canal More than two thirds of the staphylococci isolated are found to be resistant to penicillin

INCIDENCE —This disease is found most often in young children with the peak of incidence at about age 6 It is especially frequent in the late winter

PREDISPOSING FACTORS —Children are particularly susceptible to this disease because the wide short eustachian tube facilitates infection of the ear Such popular sports as swimming or diving may be contributing causes Where the adenoids are enlarged and

interfere with eustachian tube drainage, there is likelihood of recurrent otitis

CLINICAL FEATURES —After a child has had an upper respiratory infection, he may develop acute pain in the ear and fever of 100–102° F Very young children may handle the affected ear and older ones will complain of abnormal resonance of the voice and mild or moderate deafness When the fever rises and the infection is more severe, the pain is very pronounced The throat is often red Otoscopic examination will show that the drum is dull and red, first along the malleus and then all over Later the drum may bulge With adults or older children one may use a tuning fork to show that air conduction in the affected ear is reduced The other ear should be inspected carefully, as it often becomes involved If the inflammation in the mastoid becomes severe the postero superior wall of the external auditory meatus sags there is a persistent discharge and the tip of the mastoid is tender Later the pinna protrudes the fever rises higher and the patient is more toxic

LABORATORY DIAGNOSIS —A culture is taken from the myringotomy knife and sensitivity tests are carried out on the organism isolated A leukocytosis is present

DIFFERENTIAL DIAGNOSIS —Furunculosis can usually be differentiated on examination with the otoscope Otitis externa has been discussed above

PREVENTION —Prompt diagnosis and treatment of upper respiratory infections in young children is the best way of preventing otitis media

TREATMENT —Early adequate antibiotic therapy may bring about complete cure and recession of the abnormal signs in the drum Incision is necessary if bulging of the drum has been present for more than 24 hours Myringotomy has been thought necessary in 1–25% of the cases in different series When this is done promptly it helps to preserve good hearing In view of the etiological bacteria initial treatment with either penicillin, erythromycin, penicillin streptomycin or sulfonamide is indicated

Again, the advantages of drainage alone over drainage plus antibiotics has been demonstrated in some series It is claimed that recovery with myringotomy alone takes fewer days than with combined antibiotics and myringotomy

PROGNOSIS —Deaths following otitis media are now extremely rare Since the introduction of sulfonamides the necessity for mastoidectomy has been reduced from 60% to 2–3% Deafness follows in 5% or less of cases and a chronic discharge in about 2%

CHRONIC SUPPURATIVE OTITIS MEDIA

PATHOLOGY —The drum is perforated Thickening and reduplication of the mucous membrane granulation tissue and fibrous tissue may all be present Adhesions may impair the movement of the ossicles There is usually a predominance of lymphocytes in the exudate Cholesteatoma a collection of cell debris and cholesterol frequently causes bone erosion which may progress through the floor of the jugular bulb

BACTERIOLOGY —When the culture is pure the causative organisms are found to be *Proteus vulgaris* 25% *Pseudomonas aeruginosa* 20% *Staphylococcus aureus* or *Staphylococcus albus* 12% and a variety of other organisms. In cases with mixed cultures the staphylococci comprise 25% of the total

INCIDENCE —The prevalence of the chronic suppurative disease is steadily falling due to better diagnosis and treatment of acute otitis media

PREDISPOSING FACTORS —Enlarged adenoidal tissue leads to frequent acute otitis media and an increased risk of the chronic disease Patients with perennial nasal allergy are particularly prone to this complication Frequently a family entrenched infection will lead to chronic suppurative otitis media in a number of the younger members

CLINICAL FEATURES —Following several attacks of acute otitis the drum ruptures and a scanty amount of discharge is found The latter is a thick foul smelling yellowish pus in all infections

except that with pseudomonas, which produces characteristic green colored pus Deafness of varying degree is found, and by tuning fork test it is shown to be obstructive in type Vertigo may occur on applying pressure over the external canal After the canal has been cleaned perforation of the drum is evident and granulation tissue polyps or cholesteatoma may also be seen

RADIOLOGY —There may be sclerosis of the mastoid cells or evidence of cholesteatoma on x ray In cases of mastoiditis clouding of the mastoid cells contrasts with the clearness of normal cells on the unaffected side Radiology must always be correlated with the clinical findings

PREVENTION —Prompt treatment of acute otitis media is the best preventative Tonsillectomy and adenoidectomy may be necessary

TREATMENT —Antibiotic treatment systematically or locally or both is indicated only when bacteriological testing facilities are available or if prompt response follows the intelligent choosing of agents The ear must be kept clean and dry all foreign bodies such as dead ossicles granulations polypi or cholesteatomata must be removed Swimming should not be allowed

Despite these forms of treatment the discharge may continue There are two main indications for operative treatment In the first situation deterioration of the general health with signs of serious complications and a decrease in hearing or a re formation of polyps should lead to a consideration of operative treatment The second indication for operation is acute mastoiditis where mastoid tenderness becomes severe, the temperature and pulse rise the pinna is pushed out and down and the patient is toxic The more frequent procedure is a modified radical mastoidectomy

PROGNOSIS —Prognosis needs to be guarded while the ear is *still draining* Mild to moderate hearing loss can occur in up to 50% of untreated cases It should be rare in patients treated properly

DISEASES OF THE EYE

In healthy eyes staphylococci, hemolytic streptococci and corynebacteria are found in that order of frequency About 20% of people have sterile conjunctivae Only 10% of the staphylococci found in healthy eyes are coagulase positive

The anterior chamber and cornea have a natural resistance but it is hard to eliminate an experimentally induced staphylococcal infection from the vitreous.

During any sort of treatment it should be remembered that tears contain no agglutinins so the defense of the normal conjunctiva depends on mechanical means and upon lysozyme Sterile dust or any other foreign body will lead to an increase in the bacterial population. A bandage by decreasing movement and increasing heat, also enhances bacterial growth.

ULCERATIVE BLEPHARITIS

Bacteriology —Hemolytic *Staphylococcus aureus* is the usual cause

Incidence —A moderately common disease with increased frequency in older age groups

Predisposing factors —Patients with this disease may suffer from recurrent sepsis in other areas the whole family may be affected. Frequently there is an underlying seborrheic condition.

Clinical picture —The patient complains of soreness and irritation with sticking of the lids in the morning Frequent rubbing of the eyes is common The cilia are surrounded by yellow crusts scales and septic spots Removal of the crusts reveals bleeding spots The lashes frequently fall out.

Treatment —Oil removes the scales most easily Various local applications such as gentian violet 2% tincture of iodine or 3% ammoniated mercury ointment may be massaged into the lid margin at regular intervals. Systemic antibiotic treatment is beneficial in some cases. All patients should be checked to see if they are

carrying the same phage type of organism in the nose and such a reservoir of re infection should be treated as noted under the treatment of carriers In familial infections, both those with sepsis and carriers should be treated at the same time

PROGNOSIS —Blepharitis may lead to loss of some or all eye lashes

STY

SYNONYM —*Hordeolum* (Latin for 'barley corn') The word sty is from Old English *styany* a riser This is an infection of the sebaceous glands of the free edges of the eyelids

BACTERIOLOGY —Eight out of 10 patients with styes carry the same phage type of staphylococcus in the nose

INCIDENCE —The eyelids are one of the commonest sites of staphylococcal infections The disease is frequent

PREDISPOSING FACTORS —This is apt to be found in the same sort of situations as lead to acne Periods of overwork and reduced general health may predispose

CLINICAL FEATURES —A sebaceous gland becomes red swollen hard and tender A yellow point of sepsis forms at the base of one of the eyelids and the edge of the lid becomes swollen The styes may appear in crops or alternate with other forms of sepsis such as acne boils or carbuncles More constitutional upset is present than might be expected Single styes heal rapidly after rupture

TREATMENT —Hot saline compresses on the back of a wooden spoon help but they may not be worth the trouble Pulling out the affected eyelash sometimes provides drainage In recurrent cases concurrent nasal treatment should be considered Staphylo coccal toxoid has been used in the past for recurrent cases

CONJUNCTIVITIS

PATHOLOGY —Hyperemia in the conjunctival vessels is accom panied by diffuse leukocyte infiltration of the conjunctiva and

some overgrowth of the epithelium There may be an associated blepharitis

BACTERIOLOGY —Staphylococci and streptococci are the predominant causes of conjunctivitis About 50% of the staphylococci are coagulase positive *Staphylococcus aureus* but *Staphylococcus albus* if present in large numbers can be a pathogen

CLINICAL FEATURES —A subjective gritty feeling is accompanied by redness of both conjunctivae by weeping and later by some mucopurulent discharge In very acute cases there is edema of the conjunctivae (chemosis) A membrane is uncommon occasionally punctuate erosions of the cornea are seen

In severe cases the preauricular node may be involved Chronic cases may last for years

LABORATORY DIAGNOSIS —Exudate or smears are collected from the anesthetized conjunctiva One slide is stained with Gram s stain and one with Wright s. Scrapings help to differentiate the causative organism in mixed cultures A swab moistened with saline or broth is used to take cultures

TREATMENT —Staphylococci are only rarely sensitive to sulfacetamide The mild and superficial cases require local treatment such as washing out with saline Deeper infections require systemic therapy Chronic and recurrent infections need prolonged chemotherapy and occasionally immunization Zinc sulfate ⅛–¼% is helpful in chronic cases

PROGNOSIS —Conjunctivitis should respond to treatment in 1–3 days

INFECTION OF THE GLOBE
(ORBITAL CELLULITIS)

PREDISPOSING FACTORS —Occasionally this follows septicemia but it usually occurs after injury or it may be spread from nasal sinuses or be postoperative

CLINICAL FEATURES —Edema of the lids and conjunctivae is soon followed by severe pain and tenderness of the eye protru

carrying the same phage type of organism in the nose and such a reservoir of re infection should be treated as noted under the treatment of carriers In familial infections both those with sepsis and carriers should be treated at the same time

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8 | DISEASES OF ANIMALS

STAPHYLOCOCCAL DISEASE *of animals is frequent enough* to be costly but transmission from animal to man is uncommon Much of the available information is quite old with further investigation even more diseases in animals may be found to be due to staphylococci The field of staphylococcal disease in animals should be explored more widely

BACTERIOLOGY —The strains obtained from animals differ in three known respects from those obtained from man Most of the pathogenic staphylococci isolated from animals produce β hemolysin while the α hemolysin is characteristic of infections in man Alpha hemolysin produces intense hemolysis immediately around the colony while the β hemolysis shows a wider outer ring of less intense clearing The latter is called the hot cold hemolysin as reincubation at 10–20° C accentuates it

Animal strains have been shown to be predominantly of the 4?D phage type In man this is an uncommon type

A new test observing opacity after growth in egg yolk broth shows most pathogenic animal strains to be egg yolk negative (no opacity) whereas most pathogenic human strains are egg yolk positive (opacity is produced) The development of opacity is believed to be due to a lipolytic enzyme

HORSES SKIN DISEASES

Staphylococcal dermatitis in animals manifests itself in many forms Classification into distinct entities is difficult

sion proptosis and difficult movement The red reflex may be lost if a vitreous abscess is present Fever and leukocytosis are found Later optic atrophy may develop, or pus may appear at the upper inner angle

TREATMENT —Sepsis of neighboring organs, such as the sinuses requires treatment Systemic antibiotic treatment with an agent likely to penetrate the ocular tissues is usually required It is best to avoid surgery unless a fluctuant area is noted

OPHTHALMIA NEONATORUM

In the weeks following the acquisition of staphylococci from a child s environment conjunctivitis may develop Sticky eye due to staphylococci in the first month of life has been found in 15% of children born at home and in 17% of those born in the hospital While an eye infection in the first week of life is unlikely to be staphylococcal those infections which occur subsequently are frequently caused by this organism In the 6 months following the first month of life a further 13% of children develop conjunctivitis

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Smith M H D Acute bacterial meningitis Pediatrics 17 258 1956

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TREATMENT —The affected areas should be excised Systemic chemotherapy is indicated

CATTLE. SUPERFICIAL STAPHYLOCOCCAL DERMATITIDES

ACNE

This disease is most commonly found in the lower part of the tail in poorly kept animals It may be widespread throughout a herd

FURUNCULOSIS

This disease is seen at the base of the teats or on the udder between them

BOTRYOMYCOSIS

Lesions are found mainly on the udder and less often on the shoulders neck and back

MASTITIS

Inflammation of the udder in cows is caused chiefly by strep tococci or staphylococci *Aerobacter aerogenes Escherichia coli* and *Pseudomonas aeruginosa* and others are less common causal agents

PATHOLOGY —A mixture of polymorphs red cells and epi thelial cells along with many staphylococci is found in the acini The infection leads to necrosis and small abscesses which are in time replaced by fibrous tissue

BACTERIOLOGY —Strains of staphylococci are toxigenic and coagulase positive *Staphylococcus aureus* Indications are that penicillin resistance is becoming more common Most milk smears show an increase in leukocytes Smears show staphylococci in 7 out of 10 milk samples which grow pathogenic staphylococci on

Acne

This disease is not uncommon in horses Heat, tenderness and a nodular consistency of the skin develop at areas of friction particularly the posterior edge but sometimes at the anterior edge of the saddle for 3-4 inches on either side of the vertebral column Moisture predisposes and the disease is more common in the summer or in tropical latitudes in the rainy season

Furunculosis

This disease occurs in the same areas as acne

Treatment —If local antiseptic lotions are not effective, local antibiotics may be tried Long term low dose parenteral antibiotics may also help

Botryomycosis

The name is from the Latin meaning cluster of grapes and fungus This is a fungating disease of the skin due to *Staphylococcus aureus* It is more properly called granulomatous staphylococcal disease

Pathology —The fibrous polypoid masses are made up of many millimeter diameter nodules which comprise many cocci in a mucinous coating Histological section reveals reddish yellow or brown gelatinous masses sometimes containing reddish white granules.

Clinical picture —Lacerations or areas abraded by harness are especially affected wounds following castration or docking may be involved Botryomycosis may be seen on the withers shoulder, back or thorax Following involvement of the spermatic cord septicemic spread may occur in about half the cases and in such cases death often follows Abscesses may be found in the myocardium, the kidneys spleen liver, adrenal uterus or bones The infected cord becomes greatly enlarged sclerotic fibrous and purulent

centers at 18–24 hours incubation (58% accurate 9% false posi tives) With further incubation for 40 hours digestion occurs (80% accurate 7% error)

A modified *Whiteside test* has been described. One drop of 4% sodium hydroxide is mixed with 5 drops of cold milk for 20 seconds if the mixture breaks up into flakes the reaction is posi tive This test is useful for herd screening as it is not easily diluted out *False positives however occur in the first few weeks of lac* tation Milk is *cultured* in the routine fashion to demonstrate pathogenic staphylococci. Pour plates are made for counting the number of organisms per cc. and may be useful in gauging the progress of treatment. Beta hemolysis is described at the beginning of this chapter

PREVENTION —Absolute surgical cleanliness is essential when preparing medications for use in the udder Instruments used must be thoroughly sterilized

Infected cows should be isolated Healthy cows should be milked first and mastitis cows last. The udders should be care fully cleaned before milking Alcohol 70% or chlorine 250 parts per million are useful for cleaning teats However as 3% of milk will neutralize the effect of chlorine some farmers prefer phenol or a quaternary ammonium compound Mastitis in a herd has been reduced by shortening the milking time from an average of 14 minutes to 5 minutes All milk should be removed at each milking

In milking trouble may be spread by plugged vacuum lines worn out pulsators or the continued machine milking of a quarter after it is dry Teat cups of milking machines or the hands of milkers may spread the disease Attention must be paid to good management

Calves should be fed pasteurized milk if the herd is infected Straw may stay infected with staphylococci indefinitely and this may be a source of continued infection

Prevention is much more important than treatment.

TREATMENT —The treatment of this disease is best approached

culture Staphylococci can also be seen in 'uninfected milk It may be that later these animals can be diagnosed as having mastitis

INCIDENCE —Mastitis increases in frequency with age Examination of milk samples showed pathogenic staphylococci in 10–75% in different studies The attack rate in a herd may vary from 1–100% of animals, depending on methods of husbandry and treatment.

PREDISPOSING FACTORS —Injuries to the udder court infection Injury may reflect inadequate bedding a platform that is too short or misuse of milking machines Muddy yards may lead to contamination of the udders The disease is particularly common at the time of parturition or of drying off

CLINICAL PICTURE —Mastitis rarely threatens life Swelling of the udder varies from mild edema to a hard painful enlargement of the whole quarter The cow may limp from pain There is a decrease in the secretion of milk, and changes in the milk occur as noted under laboratory tests

In gangrenous cases the quarter is cyanotic, and a bloody exudate drips from the teat A high fever and depression precede death When survival occurs sloughing of the tissue takes place at 4–6 weeks and healing at 10–12 weeks

Mastitis is commonest in cows during their fourth lactation with a decline in frequency thereafter Chronic mastitis causes a crooked bag due to fibrosis The presence of fibrosis is confirmed on palpation

LABORATORY TESTS —There may be a watery first milk with shred clots and pus in the first streams of milk A *strip cup* with a fine mesh wire screen and a black background will show these changes

In the *Hotis test* the infected milk becomes alkaline and changes bromthymol blue to a green color This is a screening test which is better than the strip test it can be carried out in capillary tubes in the field Pathogenic staphylococci are indicated by greenish brown or russet-colored colonies with white

function in the affected quarter occurs in a disappointingly low number of cases

Abortions

Staphylococcus albus was recovered from semen samples from a bull used to inseminate 15 cows There were 6 abortions This same organism was obtained from necrosed cotyledens or from tan pink tinged pus in 4 instances and was also obtained from 2 of the aborted cows

HOGS

Impetigo Contagiosa

This disease is of sudden onset with vesicles pustules and crusting It occurs in young pigs in the summer It is found on the head around the eyes and ears and on the flanks

Acne

This is also found but it is rare It resembles the disease as described in horses

Botryomycosis

The disease occurs rarely in swine usually occurring after castration It resembles the disease in horses

SHEEP

Furunculosis

The disease has been described in ewes and lambs In such animals the lips swelled and so did the skin of the neck and chest The wool was replaced by pea size ulcerations with a foul smelling discharge Local incision and creolin lotion improved the condition

on a herd basis, and all the cows should be treated together to avoid recurrence It is believed that 0 1 unit of penicillin per cc. of milk is sufficient to inhibit growth of susceptible pathogens An effective dose is 100 000 units of penicillin per quarter on 2 occasions 2 days apart Procaine penicillin gives effective levels in lactating cows of 0 2–2 2 units/cc, 72 hours after administra tion Penicillin in an oil water emulsion persists for 60 hours in inhibitory concentrations A combination of 1 million units of penicillin plus 1 Gm of dihydrostreptomycin by intramammary injection once daily has been recommended Certain investigators *have claimed good results with penicillin and sulfa mixtures* others have not found this Difficulty in obtaining cure is not usually related to penicillin resistance but more probably to the inaccessibility of the organism to the drug Long standing infec tions are difficult to eradicate Animals experimentally infected with coagulase positive staphylococci were not all cured even after 3 weeks of treatment The shedding of small numbers of pathogenic staphylococci indicates that infection has not been eradicated and relapse is likely Penicillin treatment of lactating quarters in the chronic phase usually produces temporary cure only, and it is best used in quarters obviously infected Eradica tion should be tried during the dry period Streptomycin and penicillin are only slightly irritating whereas gramicidin tyro-thricin and sulfonamides are moderately or markedly irritating

Bacitracin was not found to be any better than penicillin alone and was not synergistic with penicillin Aureomycin treatment did not produce better results than penicillin treatment in the same herd Even using total doses up to 1 600 mg over an 8 day period it was unsatisfactory Further treatment studies are indicated

Milk from cows receiving penicillin should not be drunk by human beings dermatitis has been reported in children who have drunk such milk

Prognosis —*With staphylococcus infection the per cent of* recoveries has been as low as 22% Mastitis causes a drop in milk production and a decrease in the length of lactation Recovery of

survive demarcation and sloughing last for months and are associated with anemia and cachexia

TREATMENT —Affected animals should be isolated and later culled Hands should be washed after handling infected animals Penicillin alone or with sulfa should be tried Vaccines have not been successful

PROGNOSIS —Mortality figures vary from 2–21% untreated. Lambs may be lost due to the diseased udder being fibrosed and useless although frequently half the udder remains functioning

ENZOOTIC STAPHYLOCOCCAL INFECTION IN YOUNG LAMBS ASSOCIATED WITH TICK BITE

This disease is associated with the presence of ticks (*Ixodes ricinus* L.) which probably act as a mechanical aid in the development of the disease rather than as true vectors It has been described in young lambs on hill farms and produces debility or death

PATHOLOGY —In the pyemic form abscesses are disseminated throughout the body

BACTERIOLOGY —The organism is a bright orange coagulase positive *Staphylococcus aureus* which produces both alpha and beta toxins The strains are related serologically and by phage type and are fully sensitive to penicillin The organism can be recovered from the local lesions or in some cases from the heart blood

INCIDENCE —On infected farms 20–30% of 2 to 4 week-old lambs have been found to be infected. Older animals have the same staphylococci present on the skin but are not affected

CLINICAL FEATURES —The sites of tick bites in young lambs become inflamed and progress to small abscesses Wounds other than tick bites that is scars of docking of castration or at the umbilicus rarely develop abscesses The disease is only seen in animals which are tick infested The organisms can be recovered

Another outbreak showed skin lesions at the poll, withers back and rump The ears were peppered with small lesions. The fleece fell out in large areas, and the skin was covered with dried serum Below this the skin was red dry and covered with small thin scales The animals scratched against the sides of the stall with their hind feet *Staphylococcus albus* was isolated The disease was reproduced in lambs by pricking the skin with culture material

TREATMENT —Spontaneous cure takes place in the majority of cases

PROGNOSIS —A very occasional death occurs

MASTITIS

SYNONYMS —Mammitis garget, bluebag

PATHOLOGY —A mixture of polymorphs, red cells and epithelial cells is found in the acini The infection leads to necrosis and small abscess or both, which later are replaced by fibrous tissue

BACTERIOLOGY —In different epidemics staphylococci or pasturella have predominated Streptococci and coliforms have been found in a few cases Staphylococci are often found in the gangrenous type

INCIDENCE —Incidence figures have varied from 2–25% in staphylococcal outbreaks

PREDISPOSING FACTORS —Injury to the teat by the lamb or from mechanical causes predispose

CLINICAL FEATURES —Some days (or weeks) after parturition the animal becomes anorexic febrile (104–106° F) and may limp because of the unilateral inflammatory involvement of the udder The leg on the affected side is swung outwards Palpation may show that the udder is very hard and creamy pus or reddish fluid may be expressed from the teat Sometimes gangrene may supervene after hours to days The animal may die In those who

CARBUNCLE

The carbuncle similar to that described in human beings occasionally develops

DEMODECTIC MANGE

Following shedding of the hair demodectic mange (due to the hair follicle mite) frequently becomes secondarily infected with *Staphylococcus aureus*

PYODERMA GANGRAENOSUM

When untreated some of the above infections may progress to *pyoderma gangraenosum* similar to the condition of the same name in humans

TREATMENT —In the above five conditions it is best to choose an antibiotic after in vitro testing of the strain concerned Penicillin streptomycin erythromycin neomycin and aureomycin have been applied as lotions creams and sprays A synthetic organic compound triocyl has been recommended as being efficacious Autogenous bacterins have also been used in doses of 3 cc IM every other day for 3 to 4 times

Enzyme preparations (Chapter 9) have been useful in cleaning up dirty ulcerated areas Radiotherapy has been used Four to six doses of 180–240 roentgens 0 1 mm of copper filter 30 cm FHD at 2–3 day intervals repeated 6–8 weeks if necessary

OTITIS EXTERNA

In dogs it can be caused by *Staphylococcus aureus* or *Staphylococcus albus* It leads to blockage of the ear canal with purulent bloody discharge Bacitracin ointment 500 units per gram liquified in the tube by holding it under hot water is injected into the ear canal This treatment is frequently effective Operation however is frequently necessary for adequate drainage Radiotherapy

from ticks on sick lambs but not from ticks on healthy animals

Some animals die in the septicemic phase before any meta static abscesses have formed

In a number of animals abscesses may cause pressure on the central nervous system leading to impairment of gait or paralysis

DIFFERENTIAL DIAGNOSIS —In Britain the disease may mimic louping ill Unfortunately louping ill, lamb dysentery or pulpy kidney may co exist and increase the diagnostic difficulties

TREATMENT —*Control of the tick population by DDT or other* dips is the main factor in control of the disease The organisms are sensitive to penicillin but the disease is difficult to diagnose in time for successful treatment. Attempts to immunize the par turient ewes were successful in transferring antibody to suckling animals, but the lambs were not protected against a challenge staphylococcal infection

BOTRYOMYCOSIS

This disease occurs rarely in sheep at the angle of the jaw, on the shoulder on the undersurface of the thighs and on the scro tum A staphylococcal induced fungating disease of the udder has been described in sheep

DOGS

ACNE

Acne occurs on the face over the bridge of the nose and on the outer parts of *the limbs or interdigital areas especially in short* haired dogs

FURUNCULOSIS

This disease is common in the same areas as acne It is found in older dogs, especially hunting and shepherd dogs Mechanical irritation frequently predisposes Paronychia occurs

Ringer's solution is better than saline Penicillin may be given but as the disease is localized to the gut bacitracin or neomycin by mouth should be effective

PROGNOSIS —Mortalities up to 100% have been reported

RABBITS

MASTITIS

SYNONYM —Blue breast

PATHOLOGY —The nature of the disease in rabbits is the same as that found in cows

BACTERIOLOGY —It is predominantly due to staphylococcus but sometimes is caused by streptococcus

PREDISPOSING FACTORS —The disease can be spread by suckling on another doe the young from an infected doe Injuries and the results of poor housing predispose

CLINICAL PICTURE —The animals are febrile inactive and anorectic The breasts are red and hot then later blue and firm

TREATMENT —Penicillin 150 000 units given once intramuscularly and repeated if necessary may cure

CHINCHILLAS

STAPHYLOCOCCAL ENTERITIS

A disease called sudden death by breeders has been shown to be due to staphylococcal enteritis

PATHOLOGY —At autopsy the lesions are confined to the gastrointestinal tract being much more obvious in the large than in the small intestine The only gross abnormality is copious liquid fecal matter in the gut Microscopically multiple areas of focal necrosis form many shallow ulcers which do not extend beyond the muscularis They are covered by a pseudomembrane of fibrin mucosal and inflammatory cells and immense numbers of gram positive cocci

has been used as described under the previous section on skin lesions in dogs.

Mastitis

This can occur in many breeds but it is most often found in Boxers

Bacteriology —The disease is due to coagulase positive *Staphylococcus aureus* in the majority of cases

Clinical features —The udder becomes engorged, red and tender There may be some decrease in milk flow, and the bitch becomes anorectic depressed and often febrile There may be a history of mastitis in a previous lactation

Treatment —Some cases have been cured by a mixture of penicillin and sulfa Prolonged treatment (up to 6 weeks) is necessary to eradicate the disease If only one gland is involved the nipple can be taped off but the pups must be very carefully observed for the first signs of enteritis

Enteritis of Nursing Puppies

Pathology —The pathology resembles that found in the human disease

Bacteriology —Coagulase positive *Staphylococcus aureus* can be isolated from the feces and vomitus

Incidence —Most or all of the pups in a litter are affected In large breeding kennels the disease may be epidemic

Clinical features —Pups suckling from a bitch with mastitis become acutely ill and toxic with a fever of about 103° F they have foamy vomitus and liquid foamy stools Abdominal pain results in crying and the frequent stools lead to excoriation of the anus

Prophylaxis —Pups and an infected mother should be separated

Treatment —Withhold food and give parenteral fluids

VESICULAR DERMATITIS

A *vesicular dermatitis* occurs in chickens There are lesions which become crusted On removal of the crusts the skin under neath is moist and granulating Lesions are common on the pos terior region of the comb and the comb tissues thicken

AVIAN STAPHYLOCOCCOSIS
(OSTEOARTHRITIS INFESTIOSA)

This is found in young geese ducks chickens turkey poults and pigeons It has also been described in young pheasants and partridges The birds are usually 5–12 weeks old and the onset coincides with the change from down to feathers

PATHOLOGY —The articular cavities (phalangeal metatarsal and tibial) and the plantar bursa contain fibrin flaked reddish green pus In some cases true osteomyelitis of the tibia is present Enteritis may be present the mucosa is hemorrhagic and may show small serosal abscesses In a few cases pyemia is associated with an enlarged spleen and abscesses in the lung When the dis ease has become chronic there is thickening of the capsule with purulent exudates in the joint cavity

BACTERIOLOGY —This is caused by *Staphylococcus aureus* or uncommonly by *Staphylococcus albus* rarely by paratyphoid Cultures can be obtained from the joints heart and bone marrow

The disease can be reproduced experimentally

PROPHYLAXIS —Isolate healthy birds and decontaminate fowl houses lofts or roosts

In pigeons overexertion due to racing injured wings due to fighting and cold quarters all predispose to wing paralysis a manifestation of staphylococcosis

INCIDENCE —In turkey flocks 2–10% may be affected It has been described throughout North and South America and Europe

PREDISPOSING FACTORS —Wounds produced by fitting specs or pick guards may be the site of entry of the staphylococci

BACTERIOLOGY —Hemolytic *Staphylococcus aureus* grow in large quantities, and the coli aerogenes bacteria are rare in stool cultures In limited examinations staphylococci were not isolated from the heart or lung

INCIDENCE —On a farm with 450 breeding animals there were *50 deaths within 6 months*

PREDISPOSING FACTORS —The disease has been known to follow the feeding of proprietary pellets containing 0 2 mg of chlortetracycline per ounce

DIAGNOSIS —This is best made by a direct smear of the feces confirmed by cultures on unselective media (see Chapter 5) such as blood agar, rather than those used for enteric pathogens

CLINICAL FEATURES —This normally alert and very active animal becomes anorectic and lethargic and droops its head Diarrhea develops consisting of frequent semisolid or liquid stools and sometimes streaks of blood In severely ill animals the ears become cold the mucous membranes are cyanosed and the animal dies quietly

TREATMENT —Bacitracin 25 units per ml and neomycin 50 units per ml, in the drinking water for 4 days have been found to be curative

MINK

Abscesses some of which are caused by staphylococci are found in the mouth of minks associated with presence of a foreign body such as barbed grass or bone Parenteral penicillin (150 000 units intramuscularly) is recommended together with incision and drainage

BIRDS

In birds occasional cases of staphylococcal disease localized to the skin have been described However a septicemic disease localizing in the joints is the predominant disease due to this organism

infection A synthetic organic compound 'Triocyl has been beneficial in superficial lesions in dogs

LOCAL ANTIBIOTICS —Penicillin streptomycin erythromycin chloramphenicol neomycin bacitracin and tetracycline have all been applied as *lotions creams and sprays The fear of producing* an allergic condition by local application of antibiotics is less acute in animals whose life span is short and whose need for further antibiotic treatment is unlikely

Penicillin ointments contain 1 000 or 2 000 units per Gm in a petrolatum base Streptomycin 50 mg and 100 000 units of penicillin in 7.5 Gm of ointment base is used mainly for instilling into infected quarters in cases of chronic bovine mastitis Erythromycin ointment is 1% in mineral oil and petrolatum base A combined ointment of erythromycin (½% with ½% of neomycin is also available A cream or ointment with 1% chloramphenicol can be used The 3% tetracycline ointment is combined with 2% xylocaine for analgesia Bacitracin ointment for animals is the same as that for humans 500 units per Gm Bacitracin can be used to saturate dressings using the material supplied for injection The usual bacitracin ointment is also available combined with 5 mg per Gm of neomycin Neomycin 2 5 mg and gramicidin 0 25 mg per Gm are supplied in a white wax white petrolatum and peanut oil base These can be used for skin eyes or external ear Neomycin 0 5% ointment is prepared with 0 5 1 0 or 2 5% hydrocortisone with 1 5% cortisone it is available as drops or ointment for eye use Triple sulfas (4% sulfathiazole 4% sodium sulfabenzamide and 4% sulfamerazine sodium) are made into a spray for topical and ophthalmic use It must be remembered however that pus contains paraminobenzoic acid which neutralizes the actions of sulfa

ANTIBIOTICS —The same principles of antibiotic treatment (Chapter 9) apply here as are discussed for human treatment

Penicillin —Penicillin is available for oral use as tablets of 50 000 or 100 000 units or crystalline penicillin G In small animals which are fasting or more than 2 hours postprandial this is

ACUTE DISEASE —The bird looks ill, is anorectic and has severe diarrhea with sulfurlike droppings A mild conjunctivitis may be noted The metatarsal and phalangeal less often the elbow joint of the wing and other joints, are hot, swollen and painful The animals may be unable to stand When the elbow is affected the wing droops Examination shows the joints to be fluctuant hot and swollen The birds may die within 2–3 days often suddenly

THE CHRONIC DISEASE —In these cases the birds are sick for 2–3 weeks The joints show all the signs of inflammation on examination and are filled with thick purulent fluid often caseous in type The systemic upset is less obvious Diarrhea is present early but is not prominent conjunctivities is common, the birds squat down on their hocks or lie with the limbs extended backwards

The birds may die from cachexia in about 2 weeks or they may gradually recover Morbidity is marked and there is dwarfism *residual thickening of the joints and an awkward gait* Abscesses and prominent superficial veins may be present in the tibial area

DIAGNOSIS —The epizootiology is characteristic with arthritis in a number of birds Bacteriological confirmation can be carried out on blood in the acute cases or on joint fluid in the chronic cases

TREATMENT —Puncture and antiseptic irrigation of the joints has been used Systemic antibiotic treatment would also be helpful

SOME NOTES ON THE TREATMENT OF STAPHYLOCOCCAL DISEASE IN ANIMALS

LOCAL APPLICATIONS —Acriflavine 1 1000 aqueous solution or Zephiran 1 100 aqueous solution are both useful they are painted or sprayed on skin lesions provided the latter are not covered by scabs Yellow mercuric ophthalmic ointment can be used for localized eye infections or small areas of impetigenous

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given in 5 times the parenteral dose Penicillin V should prove useful in animal practice Penicillin G potassium is available in 1 2 5 or 30 million unit vials For more sustained action, penicillin G procaine is made up as 300 000 units per cc. in aqueous solution The dose of penicillin by injection for small animals is 150 000–300 000 units every 12 or 24 hours In large animals it is 2 000 units per lb every 12–24 hours as a minimum dose

Streptomycin —Supplied in vials containing 1 0 Gm or 5 0 Gm of powder, this antibiotic is given intramuscularly in a dose of 6 mg per lb per day divided into 2 doses In bovine mastitis cases 1 Gm in 100 cc of sterile distilled water can be injected into stripped quarters

Erythromycin —This antibiotic is supplied in sugar-coated tablets of 100 or 200 mg or as the stearate suspension with 100 mg per 5 cc Average size dogs are given 100 mg every 6 or 8 hours and for larger breeds this dose is doubled In larger animals 2–3 mg per lb of body weight is given every 6–8 hours The levels obtained are not affected by food intake

Chloramphenicol —In capsules of 50 100 or 250 mg this is given to small animals in a dosage of 8–25 mg per lb of body weight every 8 hours For larger animals the dose is 500 mg 2 or 3 times daily

Tetracycline —When indicated in staphylococcal infections by in vitro tests dogs and cats are given 10 to 50 mg per lb per day in divided doses in 100 or 250 mg capsules Intravenously or intramuscularly the dose is 2–5 mg per lb per day In large animals the total daily oral dose is 5–10 mg per lb Intravenously or intramuscularly the total daily dose is 1–2 mg per lb in a concentration not greater than 25 mg per cc

FURTHER READING

Biesler H E and Schwarte L H *Diseases of Poultry* (3d ed Ames Iowa Iowa State College Press 1952)

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wounds (which became alkaline) and were washed out and re placed every 5 days as by this time they were ready to pupate A disagreeable tickling of the wound was prevented by covering the surrounding skin with adhesive tape Over a 6- or 7 week period as the wound healed with granulation tissue the maggots tended to die out This treatment was also used for osteomyelitis In one post war report of 89 patients most of whom had osteomyelitis there was a recurrence rate of only 5% Children responded bet ter than adults Recently an antibiotic has been isolated from maggots

AUTOGENOUS BLOOD INJECTIONS —Under anesthesia 20 or more cc. of the patient s own citrated blood was infiltrated around the margin of a carbuncle in 2–5 sites or injected intramuscularly No proof of benefit has been offered but hemoglobin has anti bacterial properties

MODERN TREATMENT

We have made progress in the treatment of staphylococcal disease but there is still a long way to go Guideposts are now evident but in each case variations in the therapeutic regimen may be necessary Many but not all patients with severe staphy lococcal disease can be cured

Preliminaries to a Plan of Treatment

A careful history should be made regarding prior sepsis in the patient and in his relatives Should some of his family have sepsis they should receive concurrent treatment both to the lesion and the nose One must ask Is this an infection acquired in the gen eral community or is it acquired as an immediate or late result of hospitalization? If the latter is true drug resistance can be expected Again Is this lesion localized or disseminated? In the person with recurrent skin sepsis an area of carriage for the causal strain of staphylococcus must be discovered In 80% of cases the causal strain is present in the patient s nose and in the remaining

9 / TREATMENT OF STAPHYLOCOCCAL DISEASES

STAPHYLOCOCCAL DISEASES have always been important to the practitioner of medicine Before the discovery of sulfa and penicillin many attempts were made to stop chronic disease or to bring about localization of acute spreading infection A brief note on these former measures follows

TREATMENTS OF HISTORICAL INTEREST

BACTERIOPHAGE —This treatment has been used in the cases of septicemia It has not been helpful, for phage cannot be sepa rated from toxin, and so more harm than good may result tech nical advances may yet prove it to be of therapeutic value

INTRAVENOUS GENTIAN VIOLET —Cure of staphylococcal sep- ticemia by intravenous gentian violet has been claimed but the blood levels reached do not kill staphylococci in vitro

ARSENIC COLLOIDAL MANGANESE AND STANOXYL —The use of arsenic has been abandoned Metallic preparations such as Col loidal Manganese and Stanoxyl (tin) have been used in the treat ment of boils without proven benefit Metals are known, however to interfere with some of the essential enzyme processes of staphy lococci

MAGGOTS —In World War I, wounds accidentally contami nated with maggots healed well This observation led to their use in treatment Maggots were first sterilized of pathogenic organ isms and fed on a nutrient broth They were applied to the

tion with staphylococci in animal experiments we have found that a short period of fasting does. In addition if oral glucose is given to the animals during the period of fasting they become even more susceptible Dermatologists have shown that a high carbohydrate intake is a predisposing cause for skin infections Long periods of intravenous feeding with glucose should therefore be avoided

FLUIDS —Clinicians in the past have felt that small blood transfusions have been beneficial Our series of patients with untreated staphylococcal septicemia (seen mainly in the preantibiotic era) showed a mortality of 95% without transfusion and 85% with transfusion Anemia occurring in systemic staphylococcal infections does not worsen the prognosis A transfusion should therefore be given only if there is a primary need for such treatment other than the staphylococcal infection

In staphylococcal enteritis the loss of potassium in the stools presents a very difficult problem in electrolyte replacement The intake and output of both Na and K should be recorded

LOCAL APPLICATIONS —

Iodine —For the preparation of the skin for surgery iodine is efficient economical and effective It has low tissue toxicity and its color clearly delineates the area treated Iodine tincture U S P contains 2% iodine and 2% sodium iodide diluted in alcohol

Zephiran (Benzalkonium chloride U S P) —This is a cationic surface active agent which may be used in a 1 1000 tincture Soap is antagonistic and zephiran is not effective against pseudomonas which is a common hospital cross contaminant

Acriflavine N F —This application in a 1 1000 concentration in 0 9% saline solution has a wide bactericidal and bacteriostatic effect not markedly interfered with by tissue fluids

TREATMENT OF INFECTED AREA OF SKIN

There are several agents available for the treatment of infected areas of skin

Diluted sodium hypochlorite solution (modified Dakin s solu

cases carriage may occur in the axilla, the groin or in the nose of the spouse or other members of the family

Treatment of the Severely Ill Patient

There is always time to take an accurate history and inquire into the points noted above A careful physical examination follows but before treatment is started cultures must be taken When septicemia or pneumonia or both are suspected two blood cultures ½–1 hour apart, a urine, a sputum and a nasal culture are recommended One or all of these will provide a strain for further testing If the patient is obtunded and in addition shows neck stiffness a C S F culture is indicated In a patient who has a high temperature and a leukocytosis and is toxic, treatment with chloromycetin and erythromycin or novobiocin should be begun immediately after cultures have been taken A patient in coma or a patient with staphylococcal pneumonia following influenza requires intravenous therapy as death may follow rapidly In the latter type of case and in staphylococcal meningitis particular attention must be paid to the symptoms and to signs of shock and a record of the blood pressure every half hour is recommended

Prophylaxis —Care must be taken to protect susceptible people such as children and debilitated patients over the age of 50 Prophylaxis means aseptic procedures rather than the use of antibiotic ' cover The use of antibiotics to prevent infection is rarely justified It usually makes certain that the ensuing infection is *resistant to* the covering antibiotic

Nursing —Particular efforts should be made to avoid the spread of infection from one patient to another and to avoid spread of the infection from one area to another on the same patient Dressings should be firmly attached and should be occlusive, contaminated clothing should be changed and the patient should understand the measures to avoid further contamination so that full co-operation can be gained

Diet —Although undernutrition does not predispose to infec

the anterior nares of carriers It is also available as an ophthalmic ointment

Tyrothricin—For topical and intranasal use, ointment and spray N F are available in concentrations of 0 5 mg per cc Higher concentrations may be irritating

Neomycin—The ointment contains 5 mg per Gm of a suit able base It is also available combined with bacitracin It can be used as a spray for treating carriers in 1–5% concentration

The use of *cortisone* locally has little to commend it except possibly where edema is excessive and interferes with function or in a rare case with the blood supply Ointments or drops are available containing neomycin or containing bacitracin com bined with cortisone

SURGICAL TREATMENT—It is difficult to treat established ab scesses with antibiotics alone An early staphylococcal infection should not be incised but after localization has occurred and fluctuation is present incision and drainage are indicated Inci sion is preferred to aspiration except in the case of septic joints Foreign bodies such as stitches sloughs or polyethylene catheters cause a five hundred fold increase in the pathogenicity of staphy lococci injected into the skin and should be removed from the wound When a patient who is receiving the antibiotic indicated by in vitro tests continues to have fever a careful search should be made for a focus of pus and when found it should be drained This may involve surgical decapsulation of an infected kidney or drainage of a perinephric abscess

Particular attention has to be paid to the care of discharging wounds which should be covered with an adhesive occlusive covering or collodion Collodion type applications are now avail able in pressurized cans If necessary they should be further cov ered with waterproof material or plastic

THE CAUSE OF DEATH FROM STAPHYLOCOCCI

Preliminary experiments in my laboratory indicate that death in mice following the injection of staphylococci by 8 different

tion) *N F*—Dissolves and destroys bacteria pus, necrotic tissue and organic debris

Gentian violet solution U S P—One per cent in 10 per cent alcohol is messy but very effective when cutaneous ulcers are infected by staphylococci It is also available as a 2% solution in water

Ammoniated mercury ointment U S P—Frequently used in the past, it is still of value, particularly in impetigo This official preparation contains 5% of the salt A 2% ammoniated mercury ointment has been used in ulcerative blepharitis or in the treatment of chronic styes

Acetic acid—One quarter per cent acetic acid is bactericidal and is convenient for use in wet soaks

Streptokinase-Streptodornase N N R—(Synonym Varidase®) This is a mixture of enzymes obtained from hemolytic streptococci which is used to lyse fibrinous and purulent exudates in draining sinuses osteomyelitis and infected wounds or ulcers These enzymes interfere with clotting and should not be used when bleeding is present

One hundred thousand units of streptokinase and 25 000 units of streptodornase with phosphate buffer is available as a powder and can be dissolved in saline

Trypsin—(Synonym Tryptar®) This is also used for nonsurgical débridement of septic ulcerations. As a powder it is applied for 30 minutes and washed off or it is applied as a moist dressing in a dilution of 250 000 units in 25 cc Severe liver dysfunction is a contraindication

Both of the above preparations are antigenic and may cause allergic reactions

Local antibiotic applications—Locally applied antibiotics frequently produce a hypersensitive reaction therefore antibiotics which at a later date might be needed for parenteral treatment should not be used locally

Bacitracin—Bacitracin U S P in 500 units per Gm of base is effective for treatment of skin lesions and for the treatment of

general reaction the injections are increased by 0 1 cc weekly up to 1 0 cc and this last dose is repeated 5 or 6 times

Published results do not prove that this treatment is beneficial However many clinicians using the method for handling problem cases of skin sepsis have recommended it highly

CORTISONE —This drug should never be used for mild or moderate infections It is now under trial in patients who are critically ill from staphylococcal infections. Cortisone is known to be the precipitating cause of approximately 20% of cases of staphylococcal septicemia in recent years so it should never be used unless the in vitro sensitivity tests of the infecting strain are known If it is used it should be given for a few days only and antibiotics should be continued for at least a week after the cortisone has been discontinued Limited studies comparing antibiotics with cortisone against antibiotics alone in the treatment of septicemia and meningitis have shown no decrease in total deaths or in deaths in the first 24 hours Superimposed infections with organisms such as *Pseudomonas aeruginosa* have occurred

GAMMA GLOBULIN —Large doses of gamma globulin along with antibiotics protect mice from staphylococcal infections which are fatal to mice receiving the antibiotics alone Gamma globulin is probably free of hepatitis virus and can do little harm and it may be beneficial to children in the first 6 months of life Children with agammaglobulinemia may be given 0 1 Gm of gamma globulin per kg of body weight intramuscularly once monthly to protect against the common infections This produces a level of approximately 100 mg per cent of gamma globulin in the serum In adults doses of 10 to 20 cc intramuscularly given alone do not protect against infectious disease in limited trials they appear to have a synergistic effect with antibiotics A rise in temperature may occur about 6 hours after the injection This medication is expensive

NORADRENALINE —From 4 to 32 cc of 1 1000 solution are added to 500 cc of saline or 5% glucose water and are given by slow intravenous infusion This is only indicated if blood pressure

routes, is the result of the accumulation of a definite number of organisms no matter in which organ this occurs It also appears that death is caused by the cocci rather than by their exotoxins I believe this is evidence in favor of draining any localized areas of pus

Systemic Treatment Other Than Antibiotics

Antitoxins —Those prepared in the horse or rabbit have been used in the treatment of staphylococcal infections Following skin testing it is given in doses of 10,000 to 100 000 units or 75 to 160 cc intravenously or intramuscularly over a period of up to 7 days Good results are claimed but are unsupported by published series

Toxoid —Staphylococcus toxin is detoxified with formalde hyde The strength is measured as the number of dermonecrotiz ing units of the toxin from which it was made The unit of toxin is the least amount which will cause an area of erythema with a central necrosis at least 5 × 5 mm in area The toxoid is sup plied in 100 units per cc and 1 000 units per cc dilutions If an intradermal skin test with 1 unit is negative the toxoid is admin istered at 2–7 day intervals starting with 0 01 cc of the 1 000 units per cc strength intramuscularly or subcutaneously In a course of 11 injections the dose is gradually increased to 1 0 cc There are no modern papers on the use of toxoid, and it is prob able that it has little to offer in the place of a carefully planned treatment schedule which includes antibiotics

Autogenous vaccines —These have been prepared for the treatment of chronic staphylococcal disease Four to six 10% horse serum or other nutrient agar slopes are seeded with the staphylococcal strain from the patient After overnight incuba tion the colonies are emulsified in 0 5% phenol saline solution and standardized by opacity reading to 1 billion (10^9) cells per cc. After further incubation for 24–48 hours, sterility tests are carried out and then are repeated following bottling

Following a preliminary negative intradermal test 0 2 cc of the vaccine is given subcutaneously If there is neither local nor

6 Treatment should be started empirically that is by an aware ness of the sensitivities of the prevalent strains of staphylococci in the particular environment but in any other than a trivial infection this approach must be confirmed by in vitro sensi tivity tests The cost of such tests is approximately equal to the expense of one day in the hospital
7 Pus must be drained. If response to treatment is inadequate a search for trapped pus should be made
8 The temperature falls like a bouncing ball therefore treat ment should not be changed too soon If the patient feels bet ter let well enough alone

Certain preferences in the use of the different antibiotics are based on theory and experience These are summarized in Tables 3 and 4 More detailed notes on use of each of these antibiotics follow Further details regarding the penetration of antibiotics into body cavities (Table 5) and the time of their peak action (Table 6) as well as the degree of resistance to antibiotics to be expected in different types of practice (Table 7) enable a physi cian to make his choice of drug intelligently When rapid effec tive treatment is required intravenous therapy may be given and to do this with more than one drug at a time an awareness of the compatibilities of these agents in solution is required This knowledge is summarized in Table 8

PENICILLIN

This is the antibiotic of choice for staphylococcal infections *Tissue components necrotic tissue and pus do not significantly* interfere with its action No penicillin dependent strains of staph ylococci occur Resistant strains are mainly found in hospitals where they are an expression of widespread cross infection with a few drug defying strains Penicillin is well absorbed with sub-cutaneous or intramuscular injections For high initial levels the crystalline drug is preferred All types of infections due to sensi tive strains respond to penicillin therapy but with meningeal in

cannot be maintained by simpler means As the blood pressure responds rapidly and markedly a careful record of the blood pressure must be kept at 5 to 30 minute intervals

ANTIBIOTICS AND SIMILAR PREPARATIONS

WHEN TO TREAT WITH ANTIBIOTICS —Small pustules are best treated by relying on the patient s natural defenses An occlusive dressing will prevent spread and may hasten healing The patient s symptoms and signs are the best guide to the need for treatment Chills fever or leukocytosis in the presence of a known staphylococcal infection usually justify systemic chemotherapy

TABLE 4 —CLASSIFICATION OF ANTI STAPHYLOCOCCAL ANTIBIOTICS

PRIMARILY BACTE ICI L	PRIMARILY BACTERIOSTATIC
Penicillin	Tetracyclines*
Streptomycin	Chloromycetin
Tyrocidin	Novobiocin
Bacitracin	Erythromycin*
Vancomycin	Oleandomycin
Kanamycin	Sulfa
Ristocetin	
Neomycin	
Furadantin	

I h gh dosag may be bact ricidal

PRINCIPLES OF ANTIBIOTIC TREATMENT

1 Antibiotics should be used only when clearly indicated
2 There is no panacea in the treatment of staphylococcal infections Skill and knowledge must be applied to the treatment of each case
3 Bactericidal antibiotics are preferred over bacteriostatic ones (Table 4)
4 Use a full dose of antibiotics for an adequate length of time
5 A pin pointed attack with a narrow spectrum drug is better than the use of a wide spectrum antibiotic

TABLE 6 —GUIDE TO ABSORPTION AND SERUM LEVELS OF ANTIBIOTICS

Anti otic	R ute	nd D	Peak Level	Per tence	E fective L ve Again S Aure	Pea Serum Level Per Single Do e
Penicillin	I M	300 000 U	½ hr	1–2 hr	1 U/cc.	8 U/cc
Procaine Penicillin	I M	300 000 U	1–2 hr	12 hr	1 U/cc.	1 5 U/cc.
Penicillin V	Oral	250 000 U	1–4 hr	3 hr	1 U/cc	1 5 U/cc.*
Streptomycin	I M	0 5 Gm	½–3 hr	6–12 hr	15 mcg /cc	20 mcg /cc
Erythromycin	Oral	250 mg 500 q 6 h	1–4 hr	4–6 hr	0 4 mcg /cc.	1–4 mcg /cc (50 mcg /cc)
Novobiocin	Oral	500 mg	2–6 hr	6–8 hr	1 mcg /cc	15–30 mcg /cc
Chloromycetin	Oral	1 Gm	2 hr	12–18 hr	1 mcg /cc	6–8 mcg /cc
Vancomycin	I V	1 Gm.	½–1 hr	24 hr	2 mcg /cc	4–8 mcg /cc
Kanamycin	I M	0 5 Gm. 1 Gm	1–2 hr 1–2 hr	4–6 hr 4–6 hr	6 mcg /cc.	20 mcg /cc 30 mcg /cc
Ristocetin	I V	1 Gm	1st hr	10–12 hr	4–8 mcg /cc	2 5–5 mcg /cc (at 8 hr)
Tetracycline	Oral	500 mg	2 hr	6–8 hr (traces 24 hr)	1 5 mcg	3–5 mcg /cc.
	I V	500 mg	½ hr	12 hr		15–30 mcg /cc
Oleandomycin	Oral	500 mg	2 hr	6–8 hr	2 3 mcg /cc	0 5–1 mcg /cc
Triacetyl Oleando	Oral	500 mg	2 hr	6–8 hr	2 3 mcg /cc	1 5–2 mcg /cc.
Bacitracin	I M	50 000 U	2 hr	6–8 hr	5 U/cc	1–3 U/cc.
Neomycin	I M	500 mg	4–6 hr	8–10 hr	10 mcg /cc	12–30 mcg /cc
Sulfadiazine	Oral	4 Gm	15–30 min	6 hr	10–15 mg %	8–15 mg %

2 5 U/ with P ll V K

TABLE 5 —PENETRATION OF ANTIBIOTICS INTO BODY FLUIDS AND CAVITIES

	Urine	Bile	Milk	Tears	Ocular Fluids	C S F *	Pericardial Fluid	Peritoneal or Ascitic Fluid	Pleural Fluid	Saliva	Prostatic Fluid	Lymph	Joint Fluid	Fetal Circulation
Penicillin	+	+	L	L	L	0	+	+	+[1]	L		+	+	L
Streptomycin	+	L		0	0	L	+	+	+[2]	0	0	0	+	+
Erythromycin	+	+	L			0		+	+		+			+
Novobiocin	+	+			+[1]	0		+	+					
Chloromycetin	+	+	+		+	+								+
Vancomycin	+	L	Prob			0	+	+	+				+	Prob
Ristocetin	+					0								
Tetracycline	+	+	+		+[1]	+		0	+	L	L			+
Bacitracin I M	+					0		+	+					
Neomycin I M	+													
Sulfamethoxpyridine	+					+		+	+				+	?+
Sulfasoxasole	+					L		+	+				+	+
Sulfadiazine	+	+	+		+	+	+	+	+		+		+	+

Key

- \+ Present
- L Low
- 0 Not present
- [1] Slowly Better if I V
- [2] Slowly but does not penetrate empyemas
- Prob Probably present

*If the meninges are inflamed the penetration of an antibiotic may be increased

TABLE 6 —Guide to Absorption and Serum Levels of Antibiotics

Anti ot	R ute and D se		Peak L vel	Per tence	E fective Level Against S Aure s	Peak Serum Level Per Single Dose
Penicillin	I M	300 000 U	½ hr	1–2 hr	1 U/cc	8 U/cc.
Procaine Penicillin	I M	300 000 U	1–2 hr	12 hr	1 U/cc.	1 5 U/cc.
Penicillin V	Oral	250 000 U	1–4 hr	3 hr	1 U/cc.	1 5 U/cc *
Streptomycin	I M	0 5 Gm	½–3 hr	6–12 hr	15 mcg /cc	20 mcg /cc
Erythromycin	Oral	250 mg	1–4 hr	4–6 hr	0 4 mcg /cc	1–4 mcg /cc.
		500 q 6 h				(50 mcg /cc)
Novobiocin	Oral	500 mg	2–6 hr	6–8 hr	1 mcg /cc	15–30 mcg /cc
Chloromycetin	Oral	1 Gm	2 hr	12–18 hr	1 mcg /cc.	6–8 mcg /cc
Vancomycin	I V	1 Gm	½–1 hr	24 hr	2 mcg /cc	4–8 mcg /cc
Kanamycin	I M	0 5 Gm	1–2 hr	4–6 hr	6 mcg./cc	20 mcg /cc
		1 Gm	1–2 hr	4–6 hr		30 mcg /cc
Ristocetin	I V	1 Gm	1st hr	10–12 hr	4–8 mcg /cc	2 5–5 mcg /cc (at 8 hr)
Tetracycline	Oral	500 mg	2 hr	6–8 hr (traces 24 hr)	1 5 mcg	3–5 mcg /cc
	I V	500 mg	½ hr	12 hr		15–30 mcg /cc
Oleandomycin	Oral	500 mg	2 hr	6–8 hr	2 3 mcg /cc	0 5–1 mcg /cc
Triacetyl Oleando	Oral	500 mg	2 hr	6–8 hr	2 3 mcg /cc	1.5–2 mcg /cc
Bacitracin	I M	50 000 U	2 hr	6–8 hr	5 U/cc	1–3 U/cc.
Neomycin	I M	500 mg	4–6 hr	8–10 hr	10 mcg /cc	12–30 mcg /cc.
Sulfadiazine	Oral	4 Gm	15–30 min	6 hr	10–15 mg %	8–15 mg %

2 5 U/cc with P illin V K

fections it is difficult, if not impossible, to get adequate levels in the cerebrospinal fluid without intrathecal injection With relatively resistant organisms the high levels required are best attained with intravenous crystalline penicillin given by continuous drip Procaine penicillin should never be given intravenously

TOXICITY —Severe anaphylactic reactions occur after the use of penicillin tablets lozenges aersol, eye ointments and wound dressings, as well as after injection Anaphylactic symptoms may develop within seconds and death may follow in a few minutes The speed of reaction may be related to accidental intravenous injection Penicillin O and G are not different antigenically

TABLE 7 —GUIDE TO THE SENSITIVITY OF STRAINS OF STAPHYLOCOCCI TO ANTIBIOTICS

	IN HOSPITAL PRACTICE	IN GENERAL PRACTICE	IN VETERINARY PRACTICE
Penicillin	*15–20%*	*70–80%*	*70–90%*
Streptomycin	30–40%	60–70%	100%
Erythromycin	70–85%	95–100%	100%
Novobiocin	90–95%	100%	100%
Chloromycetin	95%	95%	95%
Tetracycline	30–40%	60–70%	100%

Simultaneous use of antihistamines or cortisone has not proved effective and may give a false sense of security

Skin tests are a warning when they are positive, but a negative test may mislead as it gives no assurance that it is safe to use the drug Careful inquiry into previous experience with penicillin is more helpful

The first dose of parenteral or oral preparations should be given in the doctor's presence if the patient has had previous penicillin At the first sign of a reaction adrenalin should be given

Before penicillin is injected, the plunger must be pulled back to be sure that the needle is not in a vein This is particularly true of procaine penicillin because the 600 000 units of procaine penicillin contains 240 mg procaine base and more than 8 mg per

minute of procaine intravenously produces flushing dizziness and generalized numbness.

Anaphylactic shock when penicillin is taken by mouth or is otherwise absorbed should not come as a surprise There is much laboratory and clinical experience to show that a sensitized animal or man will react anaphylactically if the antigens are absorbed from the gastrointestinal tract. For example serum from

TABLE 8.—A GUIDE TO THE MIXING OF ANTIBIOTICS FOR INTRAVENOUS USE

	PENICILLIN	STREPTOMYCIN	ERYTHROMYCIN	NOVOBIOCIN	TETRACYCLINE	VANCOMYCIN	RISTOCETIN	BACITRACIN	SOD. SULFADIAZINE
Penicillin	—	C	C	C	I	I	C	C	C
Streptomycin	C	—	C	I	C	C	C	C	—
Erythromycin	C	C	—	I	C	C	C	C	C
Novobiocin	C	I	I	—	I	I	I	I	C
Chloromycetin	C	C	C	I	C	C	C	C	C
Tetracycline	I	C	C	I	—	C	C	C	C
Vancomycin	I	C	C	I	C	—	C	I	I
Ristocetin	C	C	C	I	C	C	—	I	C
Bacitracin	C	C	C	I	C	C	I	—	C
Sod Sulfadiazine	C	C	C	C	C	I	C	C	—

I = Incompatibl C = Compatibl

an egg sensitive child placed in the skin of a normal man s back will cause a wheal reaction if the man eats an egg On the other hand we know that anaphylactic sensitization to the immense variety of foods and medicines used by man everywhere is comparatively rare we do not attempt to produce anaphylaxis in the laboratory by feeding the antigen because we know that injection is much more likely to succeed.

Since penicillin is the chief antibiotic habitually given by injection there is need for information as to what the incidence of

penicillin reactions would be if it were habitually used by mouth as are the other antibiotics. This important question has not been answered Penicillin is much the best antibiotic in many situations and anything that would make its use safer is of first importance

Preparations and dosage —It is recommended that mixtures of penicillin with other drugs be avoided Crystalline penicillin G in doses of 300,000 units once or more daily is given to adults subcutaneously or intramuscularly Large doses of penicillin G intravenously—up to 80 million units a day—are sometimes needed in staphylococcal infections Intrathecally 10–20 cc of an aqueous solution with not more than 1,000 units per cc is recommended Penicillin G procaine is given to adults in 600 000 units or greater doses once daily Benzathine penicillin G 600,000 units or 1 200 000 units can be given once every 1 or 2 weeks in adults and gives satisfactory therapeutic levels

Children —Five thousand to 10 000 units per lb every 4–12 hours

Penicillin V —Phenoxymethyl penicillin is an acid salt which passes through the stomach unchanged subsequent absorption is good but not quite as good as with injection Only 35% of penicillin V given can be recovered from the urine compared with 60% of injected penicillin It is, however the most effective form of oral penicillin and compares favorably with penicillin given by injection It will probably replace parenteral therapy for all but the most serious infections

Preparations —Tablets or capsules are of 200 000 units (125 mg) or 500 000 units (300 mg)

Dose —This is to be used in dosage equal to or slightly greater than that used parenterally

The Use of Penicillin in Penicillin Resistant Infections

There are three situations in which penicillin has been effective despite in vitro tests to the contrary In some studies lesions

due to penicillin resistant staphylococci have healed when treated with penicillin almost as quickly as those due to sensitive strains In a second situation recovery from staphylococcal endocarditis has been stated to be directly related to penicillin therapy irre spective of the sensitivity of the causative strain to penicillin Lastly mice infected with a penicillin resistant strain live longer when treated with penicillin than when untreated

Any population of bacteria is made up of individual bacteria of varying sensitivity to penicillin It is possible that the majority of a population of staphylococci might be sensitive to penicillin but in vitro resistance studies would show that there is a high degree of resistance in a minority of these bacteria

In summary while in vitro tests should provide a necessary basis for treatment the use of penicillin in addition to in vitro indicated antibiotics may have some justification but the indica tions for its use in these situations does not rest on a strong foundation

Streptomycin

This is a very effective drug against sensitive staphylococci but unfortunately many strains have become resistant to it Re sistance may develop rapidly sometimes within 48 hours of the beginning of treatment Initial dosage should be adequate and higher than that subsequently used Certain strains become de pendent on streptomycin for growth and thus treatment perpetu ates rather than cures the infection In treating urinary infections with this drug the urine should be made alkaline for greater anti bacterial effect

Toxicity —Nausea vomiting and difficulty with balance may follow prolonged use but will usually gradually disappear after withdrawal of the drug A prodromal headache may give warning of the onset of toxic effects but doses under 40 Gm are usually safe Mixture of this drug with dihydrostreptomycin is not recom mended as it may cause deafness which is a more serious toxic effect than giddiness

penicillin reactions would be if it were habitually used by mouth as are the other antibiotics This important question has not been answered Penicillin is much the best antibiotic in many situations and anything that would make its use safer is of first importance

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DOSE —This is to be used in dosage equal to or slightly greater than that used parenterally

THE USE OF PENICILLIN IN PENICILLIN RESISTANT INFECTIONS

There are three situations in which penicillin has been effective despite in vitro tests to the contrary In some studies lesions

lococci are resistant Resistant bacteria do not produce a sub stance which inhibits or destroys the antibiotic Some investigators believe that the staphylococci rapidly develop resistance to eryth romycin so that it would not be the drug of choice for prolonged treatment unless the patient was obviously gaining clinical benefit Despite these disadvantages this drug is extremely useful especially in the general community

TOXICITY —Nausea vomiting and occasionally, diarrhea oc cur but usually decrease with continued usage Serious systemic toxicity has not been observed The minor gastrointestinal upset can often be overcome by dividing the dose Freedom of erythro mycin from major toxic effects is a great advantage

PREPARATIONS AND DOSAGE —There are 100 mg or 250 mg tablets for oral use Adults require 1 or 2 Gm daily in divided doses A new preparation propionyl erythromycin gives better absorption and higher serum levels Stearate or carbonate is pre pared as 100 mg per 5 ml solution for oral use in children who should receive 3–4 mg per lb body weight For intramuscular use in adults 100 mg dissolved in 2 cc of saline can be given by deep intramuscular injection but this is fairly painful No more than 4 cc should be used at one time and sites should be changed For intravenous use erythromycin lactobionate is made up in a 1% or greater dilution and may be injected directly or added to intra venous fluids One Gm daily in divided doses should be given to adults but in serious infections 4 Gm have been given Children receive a proportionate dose in accordance with their weight

OLEANDOMYCIN

SYNONYMS PA105 MATROMYCIN® ROMICIL® —This drug is effective against pneumococci streptococci and staphylococci *When combined with twice its weight of tetracycline it is called* Signemycin® (formerly Sigmamycin®)

TOXICITY —Toxicity of a serious degree has not been noted so far

PREPARATIONS AND DOSAGE —Streptomycin sulfate U S P for parenteral injection is available as 1 or 5 Gm per ampule It is given by deep intramuscular injection *Adults* receive 2–4 Gm daily in divided dosage at 6 to 12 hour intervals, usually for not more than 7–10 days Streptomycin can be given 1 Gm per liter of intravenous fluids once or twice daily Dihydrostreptomycin must *not* be given intravenously *Children* receive 10–20 mg per lb every 6 12 or 24 hours, but up to 50 mg per lb can be used

THE ERYTHROMYCIN GROUP OF ANTIBIOTICS

There are four new drugs that have closely related antibacterial spectra and show cross resistance in the test tube Cross resistance is seen in strains isolated from patients but it varies in breadth and amount These drugs—erythromycin oleandomycin carbomycin and spiramycin—have an in vitro activity weight for weight in the approximate ratio of 50 10 5 1 Their activity in the body possibly bears the same ratio of efficacy The use of one of the inferior drugs therefore may make the subsequent use of one of the superior drugs ineffective

Mixtures of the drugs in this group with tetracycline do not have any increased effect when compared with the more active compound of the mixture Sometimes the mixtures are inferior A mixture of members of the erythromycin group may also result in inferior action

ERYTHROMYCIN

SYNONYMS ILOTYCIN® ERYTHROCIN® —Only slightly soluble in water and unstable in acid solution erythromycin must be protected from gastric acid by a resistant coating Concurrent food ingestion lowers absorption It most closely resembles penicillin in its antibacterial spectrum

A hospital problem of resistance to staphylococci to this drug has now arisen In some centers 30% of coagulase positive staphy

lococci are resistant Resistant bacteria do not produce a substance which inhibits or destroys the antibiotic Some investigators believe that the staphylococci rapidly develop resistance to erythromycin so that it would not be the drug of choice for prolonged treatment unless the patient was obviously gaining clinical benefit Despite these disadvantages this drug is extremely useful especially in the general community

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TOXICITY —Toxicity of a serious degree has not been noted so far

PREPARATIONS AND DOSAGE —The drug is available in 250 mg capsules and is given to adults in 1 or 2 Gm dosage divided throughout the day The dose for children is 10–15 mg per lb in divided doses A triacetyl derivative is believed to provide higher serum levels Oleandomycin can be given intravenously to adults who require 1–2 Gm daily in divided doses, and to children (10 mg per lb in divided doses)

The place of this drug in the therapy of staphylococcal infections is so far, difficult to assess At present it is best used against erythromycin resistant strains.

CARBOMYCIN

SYNONYM MAGNAMYCIN® —This drug reaches relatively low levels in the plasma and the urine but is eliminated in high concentration in the bile

TOXICITY —Mild gastrointestinal symptoms brown tongue, skin eruptions lethargy or disorientation have been noted occasionally

PREPARATIONS AND DOSAGE —This drug is available in 100-mg and 250 mg sugar coated tablets, and it has been used in 2 0 Gm daily dosage in adults

SPIRAMYCIN

This drug is derived from a soil streptomyces in a mixture of three chemicals not yet separated There is some accumulation of the drug in the serum In the serum however, levels are often less than that required to inhibit staphylococci in vitro, and therefore it cannot be recommended for most staphylococcal disease

TOXICITY —Many patients complain of the bitter taste of the drug and a few have had mild diarrhea.

PREPARATIONS AND DOSAGE —The 0.5 Gm tablets are hygroscopic and unstable in environments that are very acid or alkaline

A loading dose of 2 Gm is followed by 1 Gm every 6 hours
In the light of our present knowledge only an occasional patient can be helped by carbomycin or spiramycin

Novobiocin

Synonyms Albamycin® Cathomycin® streptonivisin, Cardelomycin® PA 93 and Vulcamycina®—It is *not* the same as the Soviet preparation albomycin Novobiocin resistant strains of staphylococci have been described but to date these are few in number There is no cross resistance between this and other antibiotics The appearance of resistance can be delayed by the concurrent use of another effective antibiotic

Toxicity—Nausea or diarrhea are rare It is well absorbed from the intestine A maculopapular dermatitis or occasionally a diffuse erythema develops in about 10–15% of patients Skin tests do not reveal susceptible people The rash disappears promptly on discontinuing the drug but it may interfere with the long term use of novobiocin Microscopic hematuria may accompany the rash An untoward reaction such as leukopenia hematuria arthralgia or eosinophilia has been seen in 19% of the patients receiving it One fatal case of agranulocytosis caused by this drug has been described In a few patients a yellow metabolic pigment from albamycin has been found in the plasma This can be differentiated from bilirubin by washing the plasma at pH 7 5 8 with 3 volumes of chloroform and then repeating the bilirubin determination on the washed plasma A normal bilirubin value will be revealed In the presence of jaundice only a slight change in bilirubin values will occur

Preparations and dosage—The drug is supplied in 250 mg capsules of the sodium salt and is usually given 4 times a day or 8 times a day according to the severity of infection 4 Gm daily can be given to adults and a loading dose of 2 Gm may be useful The total daily dose for children usually ranges from 5–20 mg per lb of body weight divided in 3 equal portions The higher

amounts are indicated for the more severe infections Syrup of novobiocin calcium with 125 mg per 5 cc dose is available for oral administration to children Novobiocin sodium is given to adults intramuscularly or intravenously 500 mg every 12 hours The intravenous dosage for severe illness in children is 5–10 mg per lb of body weight per day, administered parenterally in 2 divided doses at intervals of 12 hours according to the severity of the infection A specially prepared vehicle containing benzyl alcohol and N N dimethyl acetamide is required and the resultant solution should be used within 48 hours *Solutions containing dextrose are incompatible with albamycin* so the antibiotic should be diluted further with 250 cc to a liter of sterile sodium chloride or *lactate or Ringer's solution for intravenous use* *When it is necessary* to use a smaller amount of fluid intravenously, the material may be diluted to a total volume of 30 cc with one of the above diluents and given slowly over a 5–10 minute period intravenously

Chloramphenicol

Synonym Chloromycetin® —Extremely stable and resistant to wide ranges of pH as well as to boiling in water chloramphenicol is effective against staphylococci and also coliforms *Hemophilus pertussis Salmonella typhosus* certain strains of Proteus Neisseriae Salmonella, Shigella and Brucella. As this drug can occasionally cause death it is wise to reserve it for life threatening infections, or extensive or complicated disease

Toxicities —A number of fatalities have occurred with this drug following aplastic anemia possibly because of the nitrobenzine group Chronic intermittent therapy with the drug and a prior history of allergic manifestations may be predisposing factors Serum iron determinations may help in predicting the onset of toxicity This serum constituent becomes elevated Minor toxic effects include occasional gastrointestinal upsets and black discoloration of the tongue This drug also may lead to an over growth of resistant organisms such as Pseudomonas

PREPARATIONS AND DOSAGE —Capsules are given to *adults* to provide a daily dose of 2 Gm and occasionally as much as 4 Gm. Chloramphenicol palmitate containing 125 mg per teaspoonful may be given to *children* in a dose of 10–20 mg per lb every 6 hours In serious infections as much as 50 mg /lb has been given. Ampules containing 250 mg per ml are available for parenteral therapy One Gm intravenously every 12 hours provides an effec tive level in adults In children 10 mg /lb every 6 hours is given The ophthalmic ointment contains 1% of active drug

RISTOCETIN

SYNONYM SPONTIN® —This comes from the actinomycete *Norcardia luria* Resistance to Ristocetin which is active against gram positive bacteria and mycobacteria is not readily acquired The drug has the advantage of being bactericidal and of being unaffected by blood serum or pH change but has the disadvantage of having to be given intravenously gamma globulin appears to enhance its action

TOXICITY —Drug fever a pruritic erythematous rash and mild diarrhea have occurred A significant neutropenia with recovery after stopping the drug has developed in 8% of patients Fre quently phlebitis develops at the site of infusion

PREPARATIONS AND DOSAGE —Supplied as a lyophilized powder in vials containing 500 mg it should be given in a solution not stronger than 1 25% not faster than 2 cc per minute Doses of 1 5–3 Gm daily are suggested for adults but up to 6 Gm daily have been given The dose should be divided into 2 or 3 parts

KANAMYCIN

SYNONYM KANTREX® —This water soluble antibiotic derived from a streptomyces is similar in many ways to neomycin but its toxic effects are about one third as severe It is bactericidal and is effective against staphylococci as well as many bowel organ

amounts are indicated for the more severe infections Syrup of novobiocin calcium with 125 mg per 5 cc dose is available for oral administration to children Novobiocin sodium is given to adults intramuscularly or intravenously 500 mg every 12 hours The intravenous dosage for severe illness in children is 5–10 mg per lb of body weight per day, administered parenterally in 2 divided doses at intervals of 12 hours according to the severity of the infection A specially prepared vehicle containing benzyl alcohol and N N dimethyl acetamide is required and the resultant solution should be used within 48 hours *Solutions containing dextrose are incompatible with albamycin* so the antibiotic should be diluted further with 250 cc to a liter of sterile sodium chloride or lactate or Ringer's solution for intravenous use When it is necessary to use a smaller amount of fluid intravenously, the material may be diluted to a total volume of 30 cc with one of the above diluents and given slowly over a 5–10 minute period intravenously

CHLORAMPHENICOL

SYNONYM CHLOROMYCETIN® —Extremely stable and resistant to wide ranges of pH as well as to boiling in water chloramphenicol is effective against staphylococci and also coliforms *Hemophilus pertussis Salmonella typhosus* certain strains of Proteus Neisseriae Salmonella, Shigella and Brucella As this drug can occasionally cause death, it is wise to reserve it for life threatening infections, or extensive or complicated disease

TOXICITIES —A number of fatalities have occurred with this drug following aplastic anemia possibly because of the nitrobenzine group Chronic intermittent therapy with the drug and a prior history of allergic manifestations may be predisposing factors Serum iron determinations may help in predicting the onset of toxicity This serum constituent becomes elevated Minor toxic effects include occasional gastrointestinal upsets and black discoloration of the tongue This drug also may lead to an over growth of resistant organisms such as Pseudomonas

of injection particularly in children. Occasional feelings of warmth flushing or chills erythematous or morbilliform rashes have been noted Chills are now less common due to further purification

PREPARATIONS AND DOSAGE —One Gm. intravenously every 12 hours in adults is recommended *In patients with impaired renal* function much higher serum concentrations are obtained Therapeutic levels in the urine but not in the blood are found after oral administration of 0 5 Gm.

THE TETRACYCLINES

SYNONYMS ACHROMYCIN® TETRACYN® TETREX® POLYCYCLINE® etc—This group of drugs has a wide antibacterial spectrum which includes the staphylococci. Many strains now encountered in hospitals unfortunately have become resistant. The drug is absorbed adequately from the intestine but enough *remains to change the bacterial flora and to predispose to super* infection with resistant staphylococci Many small doses are better absorbed than a few large ones Chlortetracycline is also called Aureomycin® and oxytetracycline is called Terramycin® There is no evidence to suggest that either of these drugs is more effective than the parent tetracycline and they may have more undesirable side effects Tetracycline phosphate or glucosamine compounds are believed to give higher blood levels at any given dosage when compared with tetracycline The glucosamine compounds are thought to give the highest levels

TOXICITY —Nausea and anorexia are common side effects and there is a tendency to prescribe antacids Incidentally aluminum hydroxide combines with this antibiotic prevents absorption and should not be used Other metallic ions will also inactivate tetracycline Post antibiotic staphylococcal diarrhea and scarlet fever have already been described

PREPARATIONS AND DOSAGE —These drugs are in capsules with 50 100 or 250 mg for oral administration. Vials containing 100

isms and tubercle bacilli There is a cross resistance with neomycin

TOXICITY —Frequent soft stools may occur Eosinophilia is found in 9–20% of cases but drug rashes and fever are rare. Auditory toxicity, most often seen in patients over 45, is slightly less than with streptomycin, and tinnitus is a warning symptom. The total dose should be kept less than 40–50 Gm to avoid ear troubles About a quarter of the patients have some evidence of renal toxicity (casts, red cells albumin or white cells in the urine) but such toxicity is largely or wholly reversible when the drug is discontinued Some neutropenia has also been described

PREPARATIONS AND DOSAGE —For staphylococcal infections (other than enteritis) the drug can be given only intramuscularly The total daily dose for children should be 8–10 mg /lb /day in divided dosage but for severe infections up to 40 mg /lb /day have been used In adults 250–500 mg can be given every 6 hours Probably no more than 1 Gm should be given at each dose and a total daily dose should not exceed 3 5 Gm The drug is supplied in rubber capped vials as 0 5 Gm /2 cc or 1 0 Gm /3 cc. for intramuscular use It is possible that it may be used orally in the future for bowel preparation for surgery or for staphylococcal enteritis

VANCOMYCIN

SYNONYM VANCOCIN® —It is derived from strains of *Streptomyces orientalis* Valuable because it has a bactericidal effect vancomycin has the disadvantage of being administrable only by the intravenous route Predominately effective against gram positive bacteria, particularly staphylococci this antibiotic interferes with streptococci but not with the gram negative flora of the stool There has been no evidence of cross resistance with any of the other antibiotics commonly used This has proved to be a useful drug in patients resistant to treatment with other antibiotics

TOXICITY —A chemical thrombophlebitis may occur at the site

TOXICITY—Parenterally injected neomycin may cause renal damage shown by albuminuria granular casts and elevation of the blood urea nitrogen It may also damage the auditory portion of the eighth cranial nerve It frequently has one or both of these undesirable side effects and should be used only where clearly indicated

PREPARATIONS AND DOSAGE—Dermatological and ophthalmic ointments contain 5 mg per Gm of base For intestinal use, 1 Gm doses are given orally every hour for 4 doses and then every 4 hours for 1 to not more than 3 days Prior to oral use a low residue diet and a saline purgative are generally recommended When given intramuscularly to adults a total daily dose of 1 Gm in divided doses is recommended for not more than 7 days It should only be used for the treatment of serious disease when clearly indicated by in vitro testing and when other drugs cannot be used

CHEMOTHERAPEUTIC AGENTS THE SULFONAMIDES

As the sole form of treatment these drugs are recommended for certain types of urinary infection bacillary dysentery meningococcal infections and trachoma Their use in staphylococcal disease is severely limited because of their inhibition by pus and because they are only bacteriostatic They may however have a place as ancillary agents in association with penicillin or other potent antistaphylococcal drug My own clinical observation suggests that penicillin and sulfa may be better than penicillin alone in septicemia Others have suggested this in pneumonia and eye diseases Detailed comparisons of the various antistaphylococcal drugs with and without sulfa drugs are awaited with interest Sulfa should not be used in diseases where the main manifestation is the formation of pus The sulfonamides were the first chemotherapeutic drugs to which the staphylococci developed resistance but this resistance has become less since the use of sulfa has decreased

250 or 500 mg of tetracycline are available for intravenous use Daily oral dose of 1–2 Gm is given to *adults* Priming doses are not used Dilutions for intravenous use should be not stronger than 5 mg per cc, and the rate of administration should not exceed 2 cc per minute *Children* receive 10–20 mg/lb every 6 hours by mouth intravenously 10 mg/lb every 8 or 12 hours

Bacitracin

This drug is effective against gram positive cocci and gram negative cocci and clostridia Bacitracin is not interfered with by blood pus necrotic tissue or large amounts of bacteria It is not absorbed from the gut but following an intramuscular injection, effective levels are found in the plasma

Toxicity —Its major toxic effect is on the kidney Lumbar aching urinary frequency and albuminuria should lead to withdrawal of the drug This toxic effect is usually reversible Gastrointestinal upset a few local petechia at the site of injection or a macular skin rash may occur

Preparations and dosage —Skin and eye ointments are available containing 500 units per Gm of base A powder is available for making topical or parenteral solutions Solutions for parenteral use contain 500–1 000 units per cc The dose in adults by the intramuscular route should not be in excess of 100 000 units given in divided doses, and in children this dose should not exceed 500 units per lb

Neomycin

Neomycin is most useful for topical application or in the sterilization of the bowel Pus exudates gastrointestinal secretions bacterial growth *products and enzymes do not inactivate the drug* About 97% of an oral dose escapes absorption and is eliminated unchanged in the feces The drug is readily absorbed after intramuscular *injection* but *it is rapidly excreted in the urine*

TOXICITY —Parenterally injected neomycin may cause renal damage shown by albuminuria granular casts and elevation of the blood urea nitrogen It may also damage the auditory portion of the eighth cranial nerve It frequently has one or both of these undesirable side effects and should be used only where clearly indicated

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SULFADIAZINE

This is the main survivor of the earlier group of sulfa drugs Adequate fluid intake is essential, and concomitant alkali is preferred by a few

SULFASOXAZOLE (GANTRISIN)

The comparatively high solubility of this drug even in neutral or slightly acid body fluids obviates the need for alkali Urinary blockage has not been described with this drug

TRIPLE SULFAPYRIMIDINES

Because of the independent solubility of each component, protection is gained against renal blockage Most triple sulfas contain sulfadiazine sulfamethazine and sulfamerazine

SULFAMETHOXYPYRIDAZINE (KYNEX®)

The activities of this drug are equal to sulfadiazine Its urinary excretion is very slow, and therefore serum levels are maintained over a long period

TOXICITY —Sulfonamides will all produce certain deleterious side effects Different preparations lead to fever rash, granulopenia, thrombocytopenia hemolytic anemia crystalluria and lower nephron nephrosis in differing degrees The newer agents in general are less toxic than their precedessors As the sulfas are excreted by glomerular filtration they should be given with caution to patients with glomerular disease

SULFADIAZINE

Drug fever and dermatitis are occasionally seen Hematuria and granulocytopenia are rare

Sulfasoxazole

Toxic manifestations with this drug are uncommon

Triple Sulfas

Renal complications are rare Drug rash and fever occur in 2% of patients with all forms of toxicity occurring in not more than 4%

Sulfamethoxypyridazine

A rash occurs in 7% of patients and fever in 4% No renal or blood complications have been reported Counting all forms of toxicity 9% of patients are affected

Prolonged use of sulfonamides should be avoided and the drug should be stopped as soon as any toxic symptom or sign appears

Preparations and dosage —Sulfadiazine is supplied in 0 5 Gm tablets or for injection as the sodium salt 2 5 Gm in 10 cc Following a loading dose of 2–4 Gm orally 1 Gm is given every 4 hours In children the dose is 50–75 mg per pound daily in divided doses but this may be raised to 100 mg in severe infections The injectable form of the drug can be given intravenously intramuscularly or subcutaneously

Sulfasoxazole is also available in 0 5 Gm tablets and it is given in the same dosage For children it is available in a chocolate syrup or raspberry suspension containing 0 5 Gm per 5 cc The intravenous preparation contains 4 Gm in 10 cc The dose for children is the same as above Triple sulfa is available in 0 5 Gm tablets or as a suspension containing 0 5 Gm per 5 cc The dose for children is again the same

Sulfamethoxypyridazine is available in tablets of 0 5 Gm or in a caramel flavored syrup containing 0 25 Gm per 5 cc and in a cherry flavored pediatric suspension (0 25 Gm per 5 cc) In adults a loading dose of 2 or 1 Gm is given and then *only* 1 Gm

or 0 5 Gm every morning In children a single daily dose of 20 mg per lb, or 40 mg if the infection is severe, is given *It is very important to note the much smaller dose used with this sulfa compared to the older sulfonamides*

NITROFURANTOIN

SYNONYM FURADANTIN —This is rapidly and completely ab sorbed from the gastrointestinal tract Poor blood levels are achieved but levels in the urine are sufficient to be bactericidal to staphylococci In a rare case the intravenous form of the drug may be helpful in staphylococcal infection

TOXICITY —About 40% of patients develop a moderate eosino philia and about 5% a rash both of which side effects subside soon after discontinuing the drug One third of those on the drug experience nausea which can be reduced by dividing the dose into smaller portions Occasionally muscular twitching or spasticity is seen after the drug is used intravenously

PREPARATIONS AND DOSAGE —The drug is available in 50 and 100 mg tablets It is given intravenously in courses up to 14 days in quantities of 75 mg per kg divided throughout the day and given with meals An intravenous solution containing 0 6% nitra furantoin can be given in 2 divided doses in a total dose of 2–3 mg /lb per 24 hours

COMBINED THERAPY

Mixtures of antibiotics in the treatment of infectious disease are indicated (*a*) to delay the emergence of resistant bacteria (*b*) for a synergistic effect (*c*) for emergency treatment of seri ously ill patients before antibiotic sensitivity tests are completed (*d*) in infections caused by more than one organism and (*e*) to lower toxic effects by reducing the dose of each of a pair of drugs

(*a*) In staphylococcal infections delayed emergence of anti

biotic resistance is minor in degree and is bought at the price of the more extensive use of antibiotics and therefore greater numbers of resistant strains to two drugs instead of one (*b*) Synergism has been shown clinically only in the treatment of some cases of staphylococcal endocarditis when a combination of penicillin and chlortetracycline or when streptomycin and oxytetracycline have been used (*c*) In the emergency treatment of life threatening staphylococcal infection a combination of erythromycin and chloromycetin has been recommended Because of the increasing number of hospital strains resistant to the first drug I prefer to use novobiocin and chloromycetin These drugs should only be used until a definitive regimen based on in vitro test can be started (*d*) In infections with another organism as well as the staphylococcus the need for additional chemotherapy will be self-evident (*e*) No studies demonstrating lowered toxic effects in the multiple drug treatment of staphylococcal infections have been published

THE CHRONIC CASE

Over a period of months or years certain individuals will have recurrent pyogenic infections with staphylococci The approach to this problem has to be on several fronts If the patient s occupation is contributory for instance as a nurse change where possible is advisable A careful family history regarding sepsis should be taken to make sure the patient has not been reinfected at home If a positive family history is obtained a survey of the phage types of staphylococci in the family is indicated In intractable cases an autogenous vaccine may help Some indefinable factor of host resistance is often involved and a vacation frequently will assist in breaking the chain of infection As a less valuable alternative some form of sunray treatment may be beneficial The methods of dealing with this problem are still inadequate

THE TREATMENT OF CARRIERS

Carriers are of importance in only three situations, namely in hospitals, in the treatment of entrenched family infections and in the treatment of the patient with refractory sepsis Ideally the carrier responsible for a given outbreak should be traced by phage typing but at present this method is available in only a few centers In certain situations therefore, all carriers of coagulase positive staphylococci will have to be treated This has the distinct disadvantage of increasing the risk of developing resistant bacteria to the agent used The correct method is to treat the carriers of dangerous strains such species control parallels the control of malaria carrying mosquitoes

The prime areas of carriage are the nose and the feces Eighty per cent of fecal carriers are also nasal carriers In problem cases other areas of skin should be searched for carriage areas of offending strains Certain carriers are infected only for short periods, as about 15% of carriers lose their strains each month In some situations a waiting policy will simplify the problem

The antibiotics that have been used locally in the nose are penicillin the tetracyclines erythromycin bacitracin neomycin and tyrothricin The latter three are preferred as they are not usually needed for the treatment of systemic infection Application to the nose of ointments containing these agents should be carried out twice daily for 10 days Nasal sprays may be better, as they penetrate deeper into the nasopharynx A follow up examination a week after the last treatment is important If any coagulase positive staphylococci are found a second course of treatment is indicated Should carriage still persist the sinuses should be examined and treated if necessary If fecal carriage is present as well as nasal carriage a suitable oral antibiotic should be used for 10 days

Certain chemicals such as Hibitane (page 28) and quaternary ammonium compounds have been used to treat the nose They have been only moderately successful and fall considerably short

of antibiotics in effectiveness Ammoniated mercury ointment or some other nonantibiotic cream may prove useful but has not yet been tried. Much work remains to be done in this field for example in the encouragement of or implantation of avirulent strains of staphylococci or of phage in the nose The present methods for the control and treatment of carriers are unsatisfactory

REASONS FOR FAILURE WITH TREATMENT

1 The *wrong drugs* may be used this can only be corrected by careful in vitro testing
2 *Re infection* may have occurred since the patient was admitted to the hospital The strain present on admission may have been replaced by the hospital epidemic strain of a new phage type Repetition of in vitro tests and a comparison of phage types will confirm this and lead to correction of treatment
3 Antibiotic treatment will be of no avail if there is a *focus* somewhere in the body requiring surgical drainage
4 In many hospital patients there is serious impairment of *natural host resistance* Very little can be done about this except to treat the primary disease
5 *Insufficient length of treatment* may lead to relapse since staphylococci may survive within polymorphs or other cells in the body which are relatively impenetrable to circulating antibiotics It is probable that with a sufficient length of treatment these cells will give up their enclosed bacteria which will then be killed by the antibiotics
6 Direct titration of the patient's own organism against his own serum may indicate *poor absorption* of antibiotics that are given orally
7 *Antagonism* between antibiotics has been shown in vitro particularly between tetracycline and penicillin but it is improbable that this happens in the human body If two drugs are used concurrently it has been the custom to give them in half their normal dosage Provided the drugs are always given in

full dosage, it is unlikely that antagonism will be a cause for failure in treatment

8 There remain *unknown factors* which interfere with treatment Only further observation and research particularly in relation to host resistance, will elucidate these other causes of failure

FURTHER READING

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